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# CASE FILES®

## Pediatrics

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## **DEDICATION**

To my father-in-law J. Yen (Tommy) Ligh,  
whose inventive genius and sense of humor are infectious,  
and in loving memory of Lillie Woo Ligh,  
my mother-in-law whose grace and beauty continue to shine.

– Eugene C. Toy

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## PREFACE

We appreciate all the kind remarks and suggestions from the many medical students over the past 3 years. Your positive reception has been an incredible encouragement, especially in light of the short life of the *Case Files*® series. In this fourth edition of *Case Files*®: *Pediatrics*, the basic format of the book has been retained. Improvements were made in updating many of the sections. New cases include sickle cell disease, rectal bleeding, juvenile idiopathic arthritis, primary syphilis, pityriasis rosacea, and congenital cataracts. We reviewed the clinical scenarios with the intent of improving them; however, their “real-life” presentations patterned after actual clinical experience were accurate and instructive. The multiple-choice questions have been carefully reviewed and rewritten to ensure that they comply with the National Board and USMLE format. Through this fourth edition, we hope that the reader will continue to enjoy learning how to diagnose and manage patients through the simulated clinical cases. It certainly is a privilege to be teachers for so many students, and it is with humility that we present this edition.

*The Authors*

## ACKNOWLEDGMENTS

The clerkship curriculum that evolved into the ideas for this edition was inspired by two talented and forthright students, Philbert Yao and Chuck Rosipal, who have since graduated from medical school. It has been a tremendous joy to work with the excellent pediatricians at the University of Texas—Houston Medical School. I am greatly indebted to my editor, Catherine Johnson, whose exuberance, experience, and vision helped to shape this series. I appreciate McGraw-Hill's believing in the concept of teaching through clinical cases, and I would like to especially acknowledge Catherine Saggese for her production expertise, Cindy Yoo for her editorial guidance, and Ridhi Mathur for her excellent production skills.

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*Eugene C. Toy, MD*



# INTRODUCTION

Mastering the cognitive knowledge within a field such as pediatrics is a formidable task. It is even more difficult to draw on that knowledge, procure and filter through the clinical and laboratory data, develop a differential diagnosis, and finally form a rational treatment plan. To gain these skills, the student often learns best at the bedside, guided and instructed by experienced teachers, and inspired toward self-directed, diligent reading. Clearly, there is no replacement for education at the bedside. Unfortunately, clinical situations usually do not encompass the breadth of the specialty. Perhaps the best alternative is a carefully crafted patient case designed to stimulate the clinical approach and decision making. In an attempt to achieve that goal, we have constructed a collection of clinical vignettes to teach diagnostic or therapeutic approaches relevant to pediatrics. Most importantly, the explanations for the cases emphasize the mechanisms and underlying principles, rather than merely rote questions and answers.

This book is organized for versatility. It allows the student “in a rush” to go quickly through the scenarios and check the corresponding answers, while allowing the student who wants more thought-provoking explanations to go at a more measured pace. The answers are arranged from simple to complex: a summary of the pertinent points, the bare answers, an analysis of the case, an approach to the topic, a comprehension test at the end for reinforcement and emphasis, and a list of references for further reading. The clinical vignettes are purposely placed in random order to simulate the way that real patients present to the practitioner. A listing of cases is included in Section III to aid the student who desires to test his or her knowledge of a specific area or who wants to review a topic, including basic definitions. Finally, we intentionally did not primarily use a multiple-choice question format in our clinical case scenarios because clues (or distractions) are not available in the real world. Nevertheless, several multiple-choice comprehension questions are included

at the end of each case discussion to reinforce concepts or introduce related topics.

## HOW TO GET THE MOST OUT OF THIS BOOK

Each case is designed to simulate a patient encounter with open-ended questions. At times, the patient's complaint is different from the most concerning issue, and sometimes extraneous information is given. The answers are organized into four different parts:

### PART I

1. **Summary:** The salient aspects of the case are identified, filtering out the extraneous information. Students should formulate their summary from the case before looking at the answers. A comparison to the summation in the answer will help to improve their ability to focus on the important data while appropriately discarding the irrelevant information—a fundamental skill in clinical problem solving.
2. A straightforward **Answer** is given to each open-ended question.
3. The **Analysis** of the case is composed of two parts:
  - a. **Objectives:** A listing of the two or three main principles that are crucial for a practitioner to manage the patient. Again, the students are challenged to make educated “guesses” about the objectives of the case upon initial review of the case scenario, which helps to sharpen their clinical and analytical skills.
  - b. **Considerations:** A discussion of the relevant points and brief approach to the specific patient.

### PART II

**Approach** to the disease process consists of two distinct parts:

- a. **Definitions:** Terminology pertinent to the disease process.
- b. **Clinical Approach:** A discussion of the approach to the clinical problem in general, including tables, figures, and algorithms.

## **PART III**

**Comprehension Questions:** Each case contains several multiple-choice questions, which reinforce the material or introduce new and related concepts. Questions about material not found in the text have explanations in the answers.

## **PART IV**

**Clinical Pearls:** Several clinically important points are reiterated as a summation of the text. This allows for easy review, such as before an examination.

# **SECTION I**

## **How to Approach Clinical Problems**

**Part 1** Approach to the Patient

**Part 2** Approach to Clinical Problem Solving

**Part 3** Approach to Reading

## Part 1. Approach to the Patient

The transition from the textbook or journal article to the clinical situation is perhaps the most challenging in medicine. Retention of information is difficult; organization of the facts and recall of these myriad of data to apply to the patient are crucial. This text aids in the process. The first step is gathering information, otherwise known as establishing the database. This consists of taking the history (asking questions), performing the physical examination, and obtaining selective laboratory and/or imaging tests.

The history is the single most important method of establishing a diagnosis. Depending on the age of the child, the information may be gathered solely from the parent, from both the parent and the child, or solely from the adolescent. The student should remember not to be misled by the diagnosis of another physician or by a family member. A statement such as “Johnnie has pneumonia and needs antibiotics” may or may not be correct; an astute clinician will keep an open mind and consider other possibilities, such as upper respiratory tract infection, aspirated foreign body, reactive airway disease, or even cystic fibrosis. The art of seeking the information in a nonjudgmental, sensitive, and thorough method cannot be overemphasized.

## HISTORY

### 1. Basic information:

- a. **Age, gender, and ethnicity** are important because some childhood illnesses occur with increased regularity at various ages, with higher frequency in one gender or, more commonly, in one ethnic group. For instance, anorexia nervosa is more common in white adolescent females, whereas complications of sickle cell anemia are more common in African-American children of both genders.
2. **Chief complaint:** This is usually the response that the patient or the patient’s family member gives to the question: “Why are you seeing the doctor today?”
3. **History of present illness:** The onset, duration, and intensity of the primary complaint, as well as associated symptoms, exacerbating and

relieving factors, and previous attempts at therapy should be determined. For children, especially adolescents, a hidden agenda must be considered; **it is not uncommon for the adolescent to actually have questions about sexuality when the stated reason for the office visit is totally unrelated.** Both positive findings (the stool was loose, voluminous, and foul-smelling) and negative findings (without blood or mucus) are appropriate.

#### 4. Past history:

- a. **Pregnancy and delivery:** The age of the mother, the number of pregnancies, the route of delivery, and the gestational age of the infant can often provide clues as to the etiology of pediatric conditions. For instance, a large, full-term infant born by cesarean delivery who then develops an increased respiratory rate and streakiness on chest radiograph is more likely to have **transient tachypnea of the newborn** than is an infant born vaginally at 28-week gestation with similar symptoms. Similarly, a history of drug use (including over-the-counter, prescription, and illicit drugs) or infections during pregnancy should be obtained.
- b. **Neonatal history:** Any problems identified in the neonatal period, such as severe jaundice, infections, feeding difficulties, and prolonged hospitalization, should be reviewed, especially for the younger pediatric patients in whom residua of these problems may remain.
- c. **Surgical history:** When, where, and for what reason the surgery was performed should be explored. Complications should be noted.
- d. **Medical history:** Whereas minor illnesses (such as occasional upper respiratory infections) can be reviewed quickly, more serious illnesses (such as diabetes mellitus) should be investigated fully. The age at diagnosis, treatments prescribed, and response to therapies can be reviewed. The number and nature of hospitalizations and complications are often important. For instance, a diabetic patient with frequent hospitalizations for ketoacidosis may indicate a lack of education of the family or underlying psychosocial issues complicating therapy. A child with a history of frequent, serious accidents should alert the physician of possible child abuse.



- e. **Developmental history:** For preschool children, a few questions about **language and fine motor, gross motor, and psychosocial skills** will provide good clues about development. For school-aged children, areas of strength and weaknesses are helpful.
5. **Allergies:** Reactions to medications should be recorded, including severity and temporal relationship to medications.
6. **Immunizations:** Dates for primary and booster series of immunizations should be recorded, preferably by reviewing the immunization cards. If the child is in school, a presumption about state laws regarding immunization completion can be made while the immunization card is being retrieved.
7. **Medications:** List the names of current medications, dosages, routes of administration and frequency, and durations of use. Prescription, over-the-counter, and herbal remedies are relevant.
8. **Sexual history of adolescents:** Details of an adolescent's sexual habits, contraceptive use, pregnancies, and sexually transmitted diseases should be determined.
- 

## CLINICAL PEARLS

- The adolescent must be treated with sensitivity, respect, and confidentiality to foster the optimal environment for medical care.
- 

9. **Family history:** Because many conditions are inherited, the ages and health of siblings, parents, grandparents, and other family members can provide important diagnostic clues. For instance, an obese child with a family history of adult-onset diabetes is at high risk for developing diabetes; early intervention is warranted.
10. **Social history:** Living arrangements, economic situations, type of insurance, and religious affiliations may provide important clues to a puzzling diagnostic case or suggest important information about the acceptability of therapeutic options.
11. **Review of systems:** A few questions about each of the major body systems allows the practitioner to ensure that no problems are

overlooked and to obtain crucial history about related and unrelated medical conditions.

## PHYSICAL EXAMINATION

1. **General appearance:** Well- versus poorly nourished; evidence of toxemia, including lethargy (defined as poor or absent eye contact and refusal to interact with environment), signs of poor perfusion, hypo- or hyperventilation, and cyanosis; or stigmata of syndromes (such as Down or Turner).
2. **Skin:** In smaller children, checking the color of the skin for evidence of pallor, plethora, jaundice, or cyanosis is important. Abnormalities such as capillary hemangiomas (eg, “stork bites” in a newborn), café-au-lait spots, pigmented nevi (eg, “Mongolian spots”), erythema toxicum, or pustular melanosis can be identified. In older children, macules, papules, vesicles, pustules, wheals, and petechiae or purpura should be described, and evidence of excoriation, crust formation, desquamation, hyperpigmentation, ulceration, scar formation, or atrophy should be identified.
3. **Vital signs:** Temperature, blood pressure (generally begin routine measurement after 3 years), heart rate, respiratory rate, height, weight, and head circumference (generally measured until age 3 years). Measurements are plotted and compared to normals for age.
4. **Head, eyes, ears, nose, mouth and throat:**
  - a. **Head:** For the neonate, the size of fontanelles and presence of overriding sutures, caput succedaneum (superficial edema or hematoma that crosses suture lines, usually located over crown), or cephalohematoma (hematoma that does not cross suture lines) should be noted. For the older child, the size and shape of the head as well as abnormalities such as swellings, depressions, or abnormal hair quality or distribution may be identified.
  - b. **Eyes:** For infants, abnormalities in the size, shape, and position of the orbits, the color of the sclera (blue sclera, for instance, may indicate osteogenesis imperfecta), conjunctival hemorrhages or abnormalities,

or the presence of iris defects (such as coloboma) may be found. The visual acuity of older children should be determined.

- c. **Ears:** For all children, abnormalities in the size, shape, and position of the ears can provide important diagnostic clues. Whereas tympanic membranes are difficult to assess in newborns, their integrity should be assessed in older children. For all children, the quality and character of discharge from the ear canal should be documented.
  - d. **Nose:** The size, shape, and position of the nose (in relation to the face and mouth) can provide diagnostic clues for various syndromes, such as a small nose in Down syndrome. Patency of the nostrils, especially in neonates who are obligate nose breathers, is imperative. Abnormalities of the nasal bridge or septum, integrity of the mucosa, and the presence of foreign bodies should be noted. A butterfly rash around the nose can be associated with systemic lupus erythematosus (SLE), and a transverse crease across the anterior portion of the nose is seen with allergic rhinitis.
  - e. **Mouth and throat:** The size, shape, and position of the mouth and lips in relation to other facial structures should be evaluated. In infants, common findings of the mouth include disruption of the palate (cleft palate syndrome), Epstein pearls (a tiny white papule in the center of the palate), and short frenulum (“tongue-tied”). For all children, the size, shape, and position of the tongue and uvula must be considered. The number and quality of teeth for age should be assessed, and the buccal mucosa and pharynx should be examined for color, rashes, exudate, size of tonsils, and symmetry.
5. **Neck:** The neck in infants usually is short and sometimes hard to evaluate. Nonetheless, the size, shape, and preferred position of the neck can be evaluated for all children. The range of motion can be evaluated by gentle movement. Symmetry of the muscles, thyroid gland, veins, and arteries is important. An abnormal mass, such as a thyroglossal duct cyst (midline above the level of the thyroid) or brachial cleft cyst (along the sternomastoid muscle), or unusual findings, such as webbing in Turner syndrome, can be identified.
6. **Chest:** General examination of the chest should include an evaluation of the size and shape of the structures along with identification of obvious abnormalities (such as supernumerary nipples) or movement with

respirations. **Respiratory rate varies according to age** and ranges from 40 to 60 breaths/min in the neonate to 12 to 14 breaths/min in the toddler. **The degree of respiratory distress can be stratified, with increasing distress noted when the child moves from subcostal to intercostal to supraclavicular to suprasternal retractions.** Palpation of the chest should confirm the integrity of the ribs and clavicles, and any swelling or tenderness in the joints. Percussion in older children may reveal abnormalities, especially if asymmetry is noted. The chest should be auscultated for air movement, vocal resonance, rales, rhonchi, wheezes, and rubs. In adolescent girls, symmetry of breast development and presence of masses or nipple discharge should be evaluated.

7. **Cardiovascular:** The precardium should be inspected for abnormal movements. The chest should be palpated for the location and quality of the cardiac impulse, and to determine if a thrill is present. The presence and quality of the first and second heart sounds, including splitting with respirations, should be noted. Murmurs, clicks, rubs, and abnormalities in rate (which vary by age) or rhythm should be identified. The peripheral perfusion, pulses, and color should be assessed.
8. **Abdominal examination:** The abdomen should be inspected to determine whether it is flat or protuberant, if masses or lesions such as striae are obvious, or if pulsations are present. In older children, the abdomen usually is flat, but in the neonate a very flat abdomen in conjunction with respiratory distress may indicate diaphragmatic hernia. The umbilicus, especially for neonates, should be evaluated for defects, drainage, or masses; a small umbilical hernia often is present and is normal. In the newborn, one umbilical vein and two umbilical arteries are normal. **In the neonate, palpation of the abdomen may reveal a liver edge about 2 cm below the coastal margin, a spleen tip, and using deep pressure, kidneys.** In older children, these structures are not usually palpable except in pathology. Depending on the history, other masses must be viewed with suspicion for a variety of conditions. Bowel sounds are usually heard throughout the abdomen except in pathology. In adolescent females, the lower abdomen should be palpated for uterine enlargement (pregnancy).
9. **Genitalia:** Examination of the male for the size and shape of the penis, testicles, and scrotum is important. The position of the urethral opening

should be assessed. In newborn girls, the labia majora usually is large and completely encloses the labia minora; the genitalia usually is highly pigmented and swollen with an especially prominent clitoris. A white discharge is usually present in the first days of life, and occasionally a blood-tinged fluid is also seen. In toddlers, examination of the genitalia can be challenging. Placing the toddler in a frog-leg position while the toddler sits in the parent's lap (or on the examination table) often allows successful viewing of external genitalia. In older girls, the knee-chest position affords an excellent view of the external genitalia. In girls outside the newborn period, the labia minora are smaller compared to the remainder of the external genitalia, and the vaginal mucosa is red and appears thin. The hymen, which is just inside the introitus, should be inspected. Abnormalities of the hymen, such as imperforation or tags, vaginal discharge, foreign bodies, and labial adhesions, may be noted. A speculum examination should be performed for sexually active adolescent girls. Tanner staging for pubertal development should be done for both boys and girls. Inguinal hernias should be identified; normalcy of anus should be confirmed.

10. **Extremities:** For all children, the size, shape, and symmetry of the extremities should be considered; muscle strength should be evaluated. Joints may be investigated for range of motion, warmth, tenderness, and redness. Normalcy of gait for age should be reviewed. For infants, recognition of dislocated hips is of critical importance, as lifelong growth abnormalities may result. For adolescents, identification of scoliosis is important to prevent the debilitating complications of that condition. Athletes require evaluation of the integrity of their joints, especially those joints that will be used in sporting activities.
11. **Neurologic:** Neurologic evaluation of the older child is similar to that in adults. Consciousness level and orientation are determined as a starting point. The cranial nerves should be assessed. The motor system should be evaluated (including strength, tone, coordination, and involuntary movements). Superficial and deep sensory systems, and deep tendon reflexes should be reviewed. **In younger infants a variety of normal primitive reflexes (Moro, parachute, suck, grasp) can be found, but ensuring that these reflexes have extinguished by the appropriate age is equally important.**

# LABORATORY ASSESSMENT

The American Academy of Pediatrics recommends a few laboratory screening tests be accomplished for pediatric patients. These tests vary according to the child's age and risk factors.

1. **Newborn metabolic screening** is done in all states, usually after 24 hours of age, but the exact tests performed vary by state. Conditions commonly screened for include hypothyroidism, phenylketonuria, galactosemia, hemoglobin type, and adrenal hyperplasia. Other conditions that may be assessed include maple syrup urine disease, homocystinuria, biotinidase deficiency, cystic fibrosis, tyrosinemia, and toxoplasmosis. Some states require a second newborn screen be performed after 7 days of age.
2. **Hemoglobin or hematocrit levels** are recommended for high-risk infants (especially premature infants and those with low birth weight), at 9 to 12 months of age, and yearly on all menstruating adolescents.
3. **Urinalyses** are recommended at 9 to 12 months of age and at 5 years of age, and dipstick urinalysis for leukocytes annually for sexually active adolescents.
4. **Lead screening** is done, especially in high-risk areas, at 9 to 12 months of age, and again at 2 years of age.
5. **Cholesterol screening** is performed in high-risk patients (those with positive family histories) older than 24 months.
6. **Sexually transmitted disease screening** is performed yearly on all sexually active patients.

Other specialized testing is accomplished depending on the child's age, risk factors, chief complaint, and conditions included in the differential diagnosis.

# IMAGING PROCEDURES

1. **Plain radiographs** offer the advantage of inexpensive testing that reveals global views of the anatomy. Unfortunately, fine organ detail is not revealed sometimes, requiring further radiographic study. Bone films for



fracture, chest films for pneumonia, and abdomen films for ileus are common uses of this modality.

2. **Ultrasonography** is a fairly inexpensive modality that requires little or no sedation and has no radiation risks. It offers good organ and anatomic detail, but it can be operator dependent. Not all organs are accessible to sonography. Common examinations include the head for intraventricular hemorrhage (IVH) in the premature infant, the abdomen for conditions such as pyloric stenosis, and the kidneys for abnormal structure.
3. **Computer tomography (CT)** provides good organ and anatomic detail and is quick, but it is fairly expensive, may require contrast, and does involve radiation. Some children require sedation to complete the procedure. This test is often performed on the abdomen or head in trauma victims.
4. **Magnetic resonance imaging (MRI)** is expensive but does not involve radiation. Because it is a slow procedure, sedation is often needed for younger children, and contrast is sometimes required. It allows for superb tissue contrast in multiple planes, and excellent anatomic and functional imaging. It is frequently used to provide detail of the brain in patients with seizures or developmental delay, or to provide tissue detail on a mass located virtually anywhere in the body.
5. **Nuclear scan** is moderately expensive and invasive. It provides functional information (usually organ specific) but provides poor anatomic detail. Radiation is involved. Common uses include bone scans for infection and renal scans for function.

## Part 2. Approach to Clinical Problem Solving

There are generally **four steps** to the systematic solving of clinical problems:

1. Make the diagnosis
2. Assess the severity of the disease
3. Render a treatment based on the stage of the disease
4. Follow the response to the treatment

## MAKING THE DIAGNOSIS

This is achieved with careful sifting of the database, analysis based on the risk factors present, and development of a list of possibilities (the differential diagnosis). The process includes knowing which pieces of information are more meaningful and which can be discarded. Experience and knowledge from reading help to guide the physician to key in on the most important concerns. **A good clinician also knows how to ask the same question in several different ways and using different terminology,** because patients at times will deny having been treated for asthma but will answer affirmatively to being hospitalized for wheezing. A diagnosis can be reached by systematically reviewing each possible cause and reading about each disease. The patient's presentation is then matched up against each of these possibilities and either placed higher up on the list as a potential etiology or lower down because of the disease frequency, the patient's presentation, or other clues. A patient's risk factors may influence the probability of a diagnosis. Usually a long list of possible diagnoses can be pared down to two or three top suspicions, based on key laboratory or imaging tests. For example, an adolescent presenting with a fever as the chief complaint can have an extensive differential diagnosis reduced to far fewer possibilities when the history reveals an uncle in the home with cough, weight loss, and night sweats, and the physical examination shows an increased respiratory rate, lymphadenopathy, and right lower lobe lung crackles. In this case, the patient likely has tuberculosis.

## ASSESSING THE SEVERITY OF THE DISEASE

The next step is to characterize the severity of the disease process. In asthma, this is done formally based on guidelines promulgated by the National Heart, Lung, and Blood Institute (NHLBI). Asthma categories range from mild intermittent (least severe) to severe persistent (most severe). For some conditions, such as syphilis, the staging depends on the length of time and follows along the natural history of the infection (ie, primary, secondary, or tertiary syphilis).

## RENDERING TREATMENT BASED ON THE STAGE OF THE DISEASE

Many illnesses are stratified according to severity because prognosis and treatment vary based on the severity. If neither the prognosis nor the treatment was affected by the stage of the disease process, it would not make much sense to subcategorize something as mild or severe. As an example, mild intermittent asthma poses less danger than does severe persistent asthma (particularly if the patient has been intubated for asthma in the past). Accordingly, with mild intermittent asthma, the management would be intermittent short-acting  $\beta$ -agonist therapy while watching for any worsening of the disease into more serious categories (more severe disease). In contrast, a patient with severe persistent asthma would generally require short-acting  $\beta$ -agonist medications as well as long-acting  $\beta$ -agonists, inhaled steroids, and potentially oral steroids.

Group A  $\beta$ -hemolytic streptococcal pharyngeal infection (“strep throat”) is associated with complications including poststreptococcal glomerulonephritis and rheumatic fever. The presence of group A  $\beta$ -hemolytic streptococcus confers an increased risk of problems, but neither the prognosis nor the treatment is affected by “more” group A  $\beta$ -hemolytic streptococcus or “less” group A  $\beta$ -hemolytic streptococcus. Hence, **the student should approach new disease by learning the mechanism, clinical presentation, how it is staged, and how the treatment varies based on stage.**

## FOLLOWING THE RESPONSE TO TREATMENT

The final step in the approach to disease is to follow the patient's response to the therapy. **Whatever the “measure” of response, it should be recorded and monitored.** Some responses are clinical, such as a change in the patient's pain level or temperature, or results of pulmonary examination. Obviously the student must work on being more skilled in eliciting the data in an unbiased and standardized manner. Other patients may be followed by imaging, such as computerized tomography (CT) scan of a retroperitoneal (RP) node size in a patient receiving chemotherapy for neuroblastoma, or a marker such as the platelet count in a patient recovering from Kawasaki syndrome. For syphilis, it may be the nonspecific treponemal antibody test rapid plasma reagin (RPR) titer every month. The student must know what to do if the measured marker does not respond according to the expected. Is the next step to treat further, or to repeat the metastatic workup, or to follow up with another more specific test?

## **Part 3. Approach to Reading**

The student must approach reading differently than the classic “systematic” review of a particular disease entity. Patients rarely arrive to their healthcare provider with a clear diagnosis; hence, the student must become skilled in applying the textbook information to the clinical setting. Everyone retains more when the reading is performed with a purpose. Experience teaches that with reading, there are several crucial questions to consider thinking clinically. They are the following:

1. What is the most likely diagnosis?
2. What should be your next step?
3. What is the most likely mechanism for this process?
4. What are the risk factors for this condition?
5. What are the complications associated with this disease?
6. What is the best therapy?

## **WHAT IS THE MOST LIKELY DIAGNOSIS?**

Establishing the diagnosis was discussed in the previous part. This is a difficult task to give to the medical student; however, it is the basic problem that will confront clinicians for the rest of their careers. One way of attacking this problem is to develop standard “approaches” to common clinical problems. It is helpful to memorize the most common causes of various presentations, such as “the most common cause of mild respiratory distress in a term infant born by cesarean section is retained amniotic fluid (transient tachypnea of the newborn).”

The clinical scenario would entail something such as:

“A 3-hour-old infant is noted to have a mildly increased respiratory rate and slight subcostal retractions. The infant is term, large for gestation age, and was born by repeat cesarean section. The pregnancy was uncomplicated. What is the most likely diagnosis?”

With no other information to go on, the student would note that this baby has respiratory distress. Using the “most common cause” information, the

student would guess transient tachypnea of the newborn. If, instead, the gestational age “term” is changed to “preterm at 30 weeks’ gestation,” a phrase can be added, such as:

“The mother did not receive prophylactic steroids prior to birth.”

Now, the student would use the “most common cause of respiratory distress in a pre-term child whose mother did not receive prenatal steroids” is surfactant deficiency (respiratory distress syndrome).

## WHAT SHOULD BE YOUR NEXT STEP?

This question in many ways is even more difficult than the most likely diagnosis, because insufficient information may be available to make a diagnosis and the next step may be to pursue more diagnostic information. Another possibility is that the diagnosis is clear, but the subsequent step is the staging of the disease. Finally, the next step may be to treat. Hence, from clinical data, a judgment needs to be rendered regarding how far along one is on the road of:

**Make diagnosis → Stage disease → Treatment based on the stage →  
Follow response**

In particular, the student is accustomed to regurgitating the same information that someone has written about a particular disease but is not skilled at giving the next step. This talent is optimally learned at the bedside, in a supportive environment, with freedom to take educated guesses, and with constructive feedback. The student in assessing a child in the hospital should go through the following thinking process:

1. Based on the information I have, I believe that Cedric Johnson (a 3-month-old child with a positive respiratory syncytial virus nasal washing) has bronchiolitis.
2. I don’t believe that this is severe disease (such as significant oxygen requirement, severe retractions, or carbon dioxide retention on blood gas analysis). A chest radiograph shows no lobar consolidation (I believe this is important because a lobar consolidation would suggest a bacterial etiology).

3. Therefore, the treatment is supportive care with supplemental oxygen and intravenous fluids as needed.
4. I want to follow the treatment by assessing Cedric's respiratory status (I will follow the oxygen saturation and degree of retractions), his temperature, and his ability to maintain his hydration orally without intravenous fluids. Also, if in the next few days Cedric does not get better or if he worsens, I think he will need a repeat chest radiograph to assess whether he has an evolving bacterial pneumonia.

In a similar patient, when the clinical presentation is not so clear, perhaps the best “next step” may be diagnostic in nature such as blood cultures to determine if bacteremia is present. This information is sometimes tested by the dictum, “the gold standard for the diagnosis and treatment of a bacterial infection is a culture.”

Sometimes the next step is therapeutic.

## **WHAT IS THE MOST LIKELY MECHANISM FOR THIS PROCESS?**

This question goes further than requiring the student to make the diagnosis; it also requires the student to understand the underlying mechanism for the process. For example, a clinical scenario may describe a 5-year-old child with Henoch-Schönlein purpura (HSP) who develops abdominal pain and heme-positive stools a week after diagnosis. The student first must diagnose the heme-positive stools associated with HSP, which occur in approximately 50% of patients. Then, the student must understand that the edema and damage to the vasculature of the gastrointestinal (GI) tract can cause bleeding along with colicky abdominal pain, sometimes progressing to intussusception. The mechanism of the pain and bleeding is, therefore, vasculitis causing enlarged mesenteric lymph nodes, bowel edema, and hemorrhage into the bowel. Answers that a student may speculate, but would not be as likely, include appendicitis, bacterial gastroenteritis, or volvulus.

The student is advised to learn the mechanisms for each disease process and not merely to memorize a constellation of symptoms. In other words, rather than trying to commit to memory the classic presentation of HSP (typical rash, abdominal pain, and arthritis), the student should also

understand that vasculitis of the small vessels is the culprit. The vasculitis causes edema, mainly in the dependent areas, that precedes the palpable purpura. This vasculitis is responsible not only for edema in the joints (mainly in dependent areas such as the knees and ankles) causing the arthritis found in approximately two thirds of patients, but also damage to the vasculature of the GI tract leading to the intermittent, colicky abdominal pain that can manifest as heme-positive stools or even intussusception.

## **WHAT ARE THE RISK FACTORS FOR THIS CONDITION?**

Understanding the risk factors helps to establish the diagnosis and interpret test results. For example, understanding the risk factor analysis may help to manage a 1-year-old child with anemia found on routine screening. If the child had no risk factors for lead poisoning or thalassemia, the practitioner may choose to treat with supplemental iron because the likelihood for more serious pathology is low. On the other hand, if the same 1-year-old child were a recent immigrant from an endemic area, lived in a older home with peeling paint, had a father who worked at a battery smelting plant, and ate meals from unglazed pottery, a practitioner should presumptively diagnose lead poisoning until proven otherwise. The physician may want to obtain a serum lead level and a complete blood count with differential (looking for basophilic stippling), and thoroughly evaluate the child for developmental delay. Thus, the number of risk factors helps to categorize the likelihood of a disease process.

## **WHAT ARE THE COMPLICATIONS ASSOCIATED WITH THIS DISEASE?**

A clinician must understand the complications of a disease so that the patient can be monitored. Sometimes, the student will have to make the diagnosis from clinical clues and then apply his or her knowledge of the sequelae of the pathologic process. For example, a child diagnosed with high fever, rash, lymphadenopathy, and oral and conjunctival changes is diagnosed with Kawasaki syndrome. Complications of this condition include arthritis, vasculitis of the medium-sized arteries, hydrops of the gallbladder, urethritis,



and aseptic meningitis. Understanding the types of complications helps the clinician to assess the patient. For example, one life-threatening complication of Kawasaki syndrome is coronary artery aneurysm and thrombosis. **The clinical presentation in the subacute phase is desquamation, thrombocytosis, and the development of coronary aneurysms with a high risk of sudden death.** The appropriate therapy is intravenous immunoglobulin in the acute phase and high-dose aspirin as soon as possible after the diagnosis is made. Nonrecognition of the risk of coronary artery aneurysm and appropriate therapy for thrombosis can lead to the patient's death. Students apply this information when they see on rounds a patient with Kawasaki syndrome and monitor for new murmurs, thrombocytosis, myocarditis, and development of coronary artery aneurysms. The clinician communicates to the team to watch the patient for any of these signs or symptoms so that appropriate therapy can be considered.

## **WHAT IS THE BEST THERAPY?**

This is perhaps the most difficult question, not only because the clinician needs to reach the correct diagnosis, and assess the severity of the condition, but also because he or she must weigh the situation to reach the appropriate intervention. The student does not necessarily need to memorize exact dosages, but the medication, the route of delivery, and possible complications are important. It is important for the student to verbalize the diagnosis and the rationale for the therapy. A common error is for the student to “jump to a treatment,” almost like a random guess, and therefore be given a “right or wrong” feedback. In fact, the student's guess may be correct but for the wrong reason; conversely, the answer may be a very reasonable one, with only one small error in thinking. It is crucial instead to give the steps so that feedback can be given for each step.

For example, what is the best therapy for a 15-year-old sexually active girl with severe, cystic acne? The incorrect manner of response is for the clinician to blurt out “Accutane.” Rather, the student should reason it as follows:

“Severe, cystic acne can be treated with a variety of modalities. Side effects of the medications must be considered in a sexually active teenager who is statistically at high risk for pregnancy. Accutane causes severe birth

defects and is absolutely contraindicated in pregnancy. Therefore, the best treatment for this adolescent may be a combination of oral antibiotics and topical medications that present a much lower chance of devastating side effects.”

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## SECTION II

### Clinical Cases

#### CASE 1

A mother brings her 12-month-old child, a new patient for your clinic, for a well-child visit. You immediately note the child to be small for her age. Her weight is below the 5th percentile on standardized growth curves (50th percentile for an 8-month-old), her length is at the 25th percentile, and her head circumference is at the 50th percentile. Her vital signs and her examination otherwise are normal.

- ▶ What is the next step in the management of this patient?
- ▶ What is the most likely diagnosis?
- ▶ What is the next step in the evaluation?

#### ANSWERS TO CASE 1: Failure to Thrive

*Summary:* A 12-month-old girl has poor weight gain, but no etiology is suggested on examination.

- **Next step:** Gather more information, including birth, past medical, family, social, and developmental histories. A dietary history is especially important.
- **Most likely diagnosis:** Failure to thrive (FTT), most likely “nonorganic” in etiology.
- **Next step in evaluation:** Limited screening laboratory testing to identify organic causes of FTT, dietary counseling, and frequent office visits to assess weight gain.

# ANALYSIS

## *Objectives*

1. Know the historical clues necessary to recognize organic and nonorganic FTT.
2. Understand the appropriate use of the laboratory in an otherwise healthy child with FTT.
3. Appreciate the treatment and follow-up of a child with nonorganic FTT.

## *Considerations*

This patient's growth pattern (inadequate weight gain, potentially modest length retardation, and head circumference sparing) suggests FTT, most likely nonorganic given that the examination is normal. A nonorganic FTT diagnosis is made after organic etiologies are excluded, and, after adequate nutrition and an adequate environment is assured, growth resumes normally after catch-up growth is demonstrated. Diagnostic and therapeutic maneuvers aimed at organic causes are appropriate when supported by the history (prematurity, maternal infection) or examination (enlarged spleen, significant developmental delay). Although organic and nonorganic FTT can occur simultaneously, attempts to differentiate the two forms are helpful because the evaluation, treatment, and follow-up may be different.

*Note:* Had the same practitioner followed this patient since birth or had records from the previous health-care provider, earlier detection of FTT and its potential etiology might have occurred, thus allowing more rapid intervention. For instance, patients with poor caloric intake usually fail to gain weight but maintain length and head circumference. As nutrition remains poor, length becomes affected next and then ultimately head circumference.

APPROACH TO:

**Failure to Thrive**

# DEFINITIONS

**FAILURE TO THRIVE (FTT):** A physical sign, not a final diagnosis. It is suspected when a child's growth is below the 3rd or 5th percentile, in a child

less than 6 months old who does not gain weight for 2 to 3 months, or in a child whose growth crosses more than two major growth percentiles in a short time frame. Usually seen in children younger than 5 years whose physical growth is significantly less than that of their peers.

**NONORGANIC (PSYCHOSOCIAL) FTT:** Poor growth without a medical etiology. Nonorganic FTT often is related to poverty or poor caregiver–child interaction. It constitutes one-third to one-half of FTT cases identified in tertiary care settings and nearly all cases in primary care settings.

**ORGANIC FTT:** Poor growth caused by an underlying medical condition, such as inflammatory bowel disease, renal disease, or congenital heart conditions.

## CLINICAL APPROACH

The goals of the history, physical examination, and laboratory testing are to establish whether the child's caregiver is supplying enough calories, whether the child is consuming enough calories, and whether the child is able to use the calories for growth. Identification of which factor is the likely source of the problem helps guide management.

### *Diagnosis*

The history and physical examination are the most important tools in an FTT evaluation. A dietary history can offer important clues to identify an etiology. The type of milk (breast or bottle) and frequency and quality of feeding, voiding, vomiting, and stooling should be recorded. The milk used (commercial or homemade formula) and the mixing process (to ensure appropriate dilution) should be reviewed (adding too much water to powdered formula results in inadequate nutrition). The amount and type of juices and solid foods should be noted for older children. Significant food aversions might suggest gastric distress or malabsorption. A 2-week food diary (the parent notes all foods offered and taken by the child) and any associated symptoms of sweating, choking, cyanosis, difficulty sucking, and the like can be useful.

Pregnancy and early neonatal histories may reveal maternal infection, depression, drug use, intrauterine growth retardation, prematurity, or other chronic neonatal conditions. When children suspected of having FTT are seen

in families whose members are genetically small or with a slow growth history (constitutional delay), affected children are usually normal and do not require an exhaustive evaluation. In contrast, a family history of inheritable disease associated with poor growth (cystic fibrosis) should be evaluated more extensively. Because nonorganic FTT is more commonly associated with poverty, a social history is often useful. The child's living arrangements, including primary and secondary caregivers, housing type, caregiver's financial and employment status, the family's social supports, and unusual stresses (such as spousal abuse) should be reviewed. While gathering the history, the clinician can observe for unusual caregiver–child interactions.

All body organ systems potentially harbor a cause for organic FTT ([Table 1-1](#)). **The developmental status (possibly delayed in organic and nonorganic FTT) needs evaluation.** Children with nonorganic FTT may demonstrate an occipital bald spot from lying in a bed and failure to attain appropriate developmental milestones resulting from lack of parental stimulation; may be disinterested in their environment; may avoid eye contact, smiling, or vocalization; and may not respond well to maternal attempts of comforting. Children with some types of organic FTT (renal tubular acidosis) and most nonorganic FTT show “catch-up” in developmental milestones with successful therapy. During the examination (especially of younger infants) **the clinician can observe a feeding, which may give clues to maternal-child interaction bonding issues or to physical problems** (cerebral palsy, oral motor or swallowing difficulties, velum cleft palate).

### **Inadequate Caloric Intake**

- Lack of appetite: depression, chronic disease
- Ingestion difficulties: feeding disorders, neurologic disorders (cerebral palsy), craniofacial anomalies, genetic syndromes, tracheoesophageal fistula
- Unavailability of food: neglect, inappropriate food for age, insufficient volume of food

### **Altered Growth Potential**

- Prenatal insult, chromosomal anomalies, endocrine disorders

### **Caloric Wasting**

- Emesis: intestinal tract disorders, drugs, toxins, CNS pathology
- Malabsorption: GI disease (biliary atresia, celiac disease), inflammatory bowel disease, infections, toxins
- Renal losses: diabetes, renal tubular acidosis

### **Increased Caloric Requirements**

- Increased metabolism: congenital heart disease, chronic respiratory disease, neoplasms, chronic infection, hyperthyroidism
- Defective use of calories: metabolic disorders, renal tubular acidosis

*Abbreviations: CNS, central nervous system; GI, gastrointestinal.*

## **Table 1-1 • MAJOR CAUSES OF INADEQUATE WEIGHT GAIN**

The history or examination suggestive of organic FTT directs the laboratory and radiologic evaluation. In most cases, results of the newborn state screen are critical. A child with cystic fibrosis in the family requires sweat chloride or genetic testing, especially if this testing is not included on the newborn state screen. A child with a loud, harsh systolic murmur and bounding pulses deserves a chest radiograph, an electrocardiogram (ECG), and perhaps an echocardiogram and cardiology consult.

Most FTT children have few or no signs. Thus, laboratory evaluation is usually limited to a few screening tests: a complete blood count (CBC), lead level (especially for patients in lower socioeconomic classes or in cities with a high lead prevalence), thyroid and liver function tests, urinalysis and culture, and serum electrolyte levels (including calcium, blood urea nitrogen [BUN], and creatinine). A tuberculosis skin test and human immunodeficiency virus testing may also be indicated. Abnormalities in screening tests are pursued more extensively.

### ***Treatment and Follow-up***

The treatment and follow-up for organic FTT are disease specific. Patients with nonorganic FTT are managed with improved dietary intake, close follow-up, and attention to psychosocial issues.

**Healthy infants in the first year of life require approximately 120 kcal/kg/d of nutrition and about 100 kcal/kg/d thereafter; FTT children require an additional 50% to 100% to ensure adequate catch-up growth.** A mealtime routine is important. Families should eat together in a nondistracting environment (television off!), with meals lasting between 20 and 30 minutes. Solid foods are offered before liquids; children are not force-fed. Low-calorie drinks, juices, and water are limited; age-appropriate high-calorie foods (whole milk, cheese, dried fruits, peanut butter) are encouraged. Formulas containing more than the standard 20 cal/oz may be necessary for smaller children, and high-calorie supplementation (PediaSure or Ensure) may be required for larger children. Frequent office or home health visits are indicated to ensure weight gain. In some instances, hospitalization of an FTT child is required; such infants often have rapid weight gain, supporting the diagnosis of nonorganic FTT.



Nonorganic FTT treatment requires not only the provision of increased calories but also attention to contributing psychosocial issues. Referral to community services (Women, Infants, and Children [WIC] Program, Food Stamp Program, and local food banks) may be required. Caregiver help in the form of job training, substance and physical abuse prevention, parenting classes, and psychotherapy may be available through community programs. Older children and their families may benefit from early childhood intervention and Head Start programs.

Some children with organic FTT also have nonorganic FTT. For instance, a poorly growing special-needs premature infant is at increased risk for superimposed nonorganic FTT because of psychosocial issues, such as poor bonding with the family during a prolonged hospital stay. In such cases, care for the organic causes is coordinated with attempts to preclude nonorganic FTT.

## COMPREHENSION QUESTIONS

- 1.1 Parents bring their 6-month-old son to see you. He is symmetrically less than the 5th percentile for height, weight, and head circumference on routine growth curves. He was born at 30 weeks' gestation and weighed 1000 g. He was a planned pregnancy, and his mother's prenatal course was uneventful until an automobile accident initiated the labor. He was ventilated for 3 days in the intensive care unit (ICU) but otherwise did well without ongoing problems. He was discharged at 8 weeks of life. Which of the following is the mostly likely explanation for his small size?
- A. Chromosomal abnormality
  - B. Protein-calorie malnutrition
  - C. Normal ex-premie infant growth
  - D. Malabsorption secondary to short gut syndrome
  - E. Congenital hypothyroidism
- 1.2 A 13-month-old child is noted to be at the 25th percentile for weight, the 10th percentile for height, and less than the 5th percentile for head circumference. She was born at term. She was noted to have a small head at birth, to be developmentally delayed throughout her life, and to

have required cataract surgery shortly after birth. She currently takes phenobarbital for seizures. Which of the following would most likely explain this child's small size?

- A. Congenital cytomegalovirus (CMV) infection
- B. Down syndrome
- C. Glycogen storage disease type II
- D. Congenital hypothyroidism
- E. Craniopharyngioma

1.3 A 2-year-old boy had been slightly less than the 50th percentile for weight, height, and head circumference, but in the last 6 months he has fallen to slightly less than the 25th percentile for weight. The pregnancy was normal, his development is as expected, and the family reports no psychosocial problems. The mother says that he is now a finicky eater (wants only macaroni and cheese at all meals), but she insists that he eat a variety of foods. The meals are marked by much frustration for everyone. His examination is normal. Which of the following is the best next step in his care?

- A. Sweat chloride testing
- B. Ophthalmologic examination for retinal hemorrhages
- C. Reassurance and counseling for family about childhood normal developmental stage
- D. Testing of stool for parasites
- E. Magnetic resonance imaging (MRI) of the brain

1.4 A 4-month-old child has poor weight gain. Her current weight is less than the 5th percentile, height about the 10th percentile, and head circumference at the 50th percentile. The planned pregnancy resulted in a normal, spontaneous, vaginal delivery; mother and child were discharged after a 48-hour hospitalization. Feeding is via breast and bottle; the quantity seems sufficient. The child has had no illness. The examination is unremarkable except for the child's small size. Screening laboratory shows the hemoglobin and hematocrit are 11 mg/dL and 33%, respectively, with a platelet count of 198,000/mm<sup>3</sup>. Serum electrolyte levels are sodium 140, chloride 105, potassium 3.5, bicarbonate 17,

blood urea nitrogen 15, and creatinine 0.3. Liver function tests are normal. Urinalysis reveals a pH of 8 with occasional epithelial cells but no white blood cells, bacteria, protein, ketones, or reducing substances. Which of the following is the most appropriate therapy for this child?

- A. Transfusion with packed red blood cells (PRBCs)
- B. Intravenous (IV) infusion of potassium chloride
- C. Sweat chloride analysis
- D. Growth hormone determination
- E. Oral supplementation with bicarbonate

## ANSWERS

- 1.1 C. The expected weight versus age must be modified for a preterm infant. Similarly, growth for children with Down or Turner syndrome varies from that for other children. Thus, use of an appropriate growth curve is paramount. For the child in the question, weight gain should follow or exceed that of term infants. For this premature infant, when his parameters are plotted on a “premie growth chart,” normal growth is revealed.
- 1.2 A. The developmental delay, intrauterine growth retardation (including microcephaly), cataracts, seizures, hepatosplenomegaly, prolonged neonatal jaundice, and purpura at birth are consistent with a congenital cytomegalovirus (CMV) or toxoplasmosis infection. Calcified brain densities of CMV typically are found in a periventricular pattern; in toxoplasmosis, they are found scattered throughout the cortex.
- 1.3 C. Between 18 and 30 months of age children often become “picky eaters.” Their growth rate can plateau, and the period can be distressing for families. Calm counseling of parents to provide nutrition, avoid “force-feeding,” and avoid providing snacks is usually effective. Close follow-up is required.
- 1.4 E. The patient has evidence of renal tubular acidosis (probably distal tubular), a well-described cause of FTT. Upon confirmation of the findings, oral bicarbonate supplementation would be expected to correct

the elevated chloride level, the low bicarbonate and potassium levels (although potassium supplements may be required), and poor growth.

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## CLINICAL PEARLS

- In the United States, psychosocial failure to thrive is more common than organic failure to thrive; it often is associated with poverty or poor parent-child interaction.
  - Inexpensive laboratory screening tests, dietary counseling, and close observation of weight changes are appropriate first steps for most healthy-appearing infants with failure to thrive.
  - Organic failure to thrive can be associated with abnormalities of any organ system. Clues in history, examination, or screening laboratory tests help identify affected organ systems.
  - Up to one-third of patients with psychosocial failure to thrive have developmental delay as well as social and emotional problems.
  - Patients with renal tubular acidosis, a common cause of organic failure to thrive, can have proximal tubule defects (type 2) caused by impaired tubular bicarbonate reabsorption or distal tubule defects (type 1) caused by impaired hydrogen ion secretion. Type 4 is also a distal tubule problem associated with impaired ammoniogenesis.
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A healthy 16-year-old adolescent arrives at your office with his parents, who are concerned about his several months' history of erratic behavior. At times he has a great deal more energy, seems to be in a terrific mood, and has unusually high self-esteem; during these episodes he has difficulty concentrating, remembering things, and often has headaches. At other times he seems to be his "normal" self. He had previously been a good student, but his grades have fallen this year. Last evening he appeared flushed and agitated, he had dilated pupils and a rapid heart rate, and he complained "people were out to get him." The family reluctantly reports that he was arrested for burglary 2 weeks previously. You know him to be in otherwise good health. Today he appears normal.

- ▶ What is the most likely diagnosis?
- ▶ What is the next step in the evaluation?
- ▶ What is the long-term evaluation and therapy?

## ANSWERS TO CASE 2: Adolescent Substance Abuse

*Summary:* A 16-year-old previously healthy adolescent with recent behavior changes and declining school performance.

- **Most likely diagnosis:** Drug abuse (probably MDMA [ecstasy] or possibly cocaine or amphetamines).
- **Next steps in evaluation:** History, examination, urine drug screen, and screening for other commonly associated drug abuse consequences (sexually transmitted infections [STIs], hepatitis).
- **Long-term evaluation and therapy:** Threefold approach: (1) detoxification program, (2) follow-up with developmentally appropriate psychosocial support systems, and (3) possible long-term assistance with a professional trained in substance abuse management.

## ANALYSIS

### *Objectives*

1. Learn the pattern of behavior found among drug-abusing adolescents.
2. Know the signs and symptoms of the drugs most commonly abused by adolescents.
3. Understand the general approach to therapy for an adolescent abusing drugs.

### ***Considerations***

Rarely, a brain tumor could explain an adolescent with new onset of behavior changes. **In general, however, an adolescent's new-onset truant behavior, depression or euphoria, or declining grades is more commonly associated with substance abuse.** A previously undiagnosed psychiatric history (mania or bipolar disease), too, must be considered. A history, family history, physical examination (especially the neurologic and psychological portions), and screening laboratory will help provide clarity. Information can come from the patient, his family, or other interested parties (teachers, coaches, and friends). Direct questioning of the adolescent alone about substance abuse is appropriate during routine health visits or when signs and symptoms are suggestive of abuse.

### **APPROACH TO:**

#### **The Substance-Abusing Adolescent**

## **DEFINITIONS**

**SUBSTANCE ABUSE:** Alcohol or other drug use leading to impairment or distress, causing failure of school or work obligations, physical harm, substance-related legal problems, or continued use despite social or interpersonal consequences resulting from the drug's effects.

**SUBSTANCE DEPENDENCE:** Alcohol and other drug use, causing loss of control with continued use (tolerance requiring higher doses or withdrawal when terminated), compulsion to obtain and use the drug, and continued use despite persistent or recurrent negative consequences.

## **CLINICAL APPROACH**

Experimentation with alcohol and other drugs is common among adolescents; some consider this experimentation “normal.” Others argue it is to be avoided because substance abuse is often a cause of adolescent morbidity and mortality (homicide, suicide, and unintentional injuries). In all cases, a health-care provider is responsible for discussing facts about alcohol and drugs in an attempt to reduce the adolescent’s risk of harm and for identifying those requiring intervention.

Children at risk for drug use include those with significant behavior problems, learning difficulties, and impaired family functioning. Cigarettes and alcohol are the most commonly used drugs; marijuana is the most commonly used illicit drug. Some adolescents abuse common household products (inhalation of glue or aerosols); others abuse a sibling’s medications (methylphenidate, which is often snorted with cocaine).

The American Academy of Pediatrics (AAP) recommends pediatricians ask about alcohol or drug use during the adolescent’s annual health examination or when an adolescent presents with evidence of substance abuse. Direct questions can identify drug or alcohol use and their effect on school performance, family relations, and peer interactions. Should problems be identified, an interview to determine the degree of drug use (experimentation, abuse, or dependency) is warranted.

**Historical clues to drug abuse include significant behavioral changes at home, a decline in school or work performance, or involvement with the law.** An increased incidence of **intentional or accidental injuries** may be alcohol or drug related. Risk-taking activities (trading sex for drugs, driving while impaired) can be particularly serious and may suggest serious drug problems. Alcohol or other drug users usually have a normal examination, especially if the use was not recent. Needle marks and nasal mucosal injuries are rarely found.

An adolescent with recent alcohol or drug use can present with a variety of findings ([Table 2-1](#)). A urine drug screen (UDS) can be helpful to evaluate the adolescent who: (1) presents with psychiatric symptoms, (2) has signs and symptoms commonly attributed to drugs or alcohol, (3) is in a serious accident, or (4) is part of a recovery monitoring program. **An attempt to obtain the adolescent’s permission and maintain confidentiality is paramount.**



Agent	Signs and Symptoms	Retention Time for Urine Screening Purposes
Alcohol	Euphoria, grogginess, impaired short-term memory, talkativeness, vasodilation, and at high serum alcohol levels, respiratory depression	7-10 h (blood) or 10-13 h (urine)
Marijuana	Elation and euphoria, impaired short-term memory, distortion of time perception, poor performance of tasks requiring concentration (such as driving), and loss of judgment	3-10 d for occasional users or up to 2 mo for chronic users
Cocaine	Euphoria, increased motor activity, decreased fatigability, dilated pupils, tachycardia, hypertension and hyperthermia; sometimes associated with paranoid ideation; physical findings might include changes in nasal mucosa	2-4 d
Methamphetamine and	Euphoria, increased sensual awareness,	2 d

methylenedioxymethamphetamine (ecstasy)	increased psychic and emotional energy, nausea, teeth grinding, tachycardia, blurred vision, jaw clenching, anxiety, panic attacks, and psychosis	
Opiates including heroin, morphine, and codeine	Euphoria, decreased pain sensation, pinpoint pupils, hypothermia, vasodilation, and possible respiratory depression; physical findings might include needle marks over veins	2 d
Phencyclidine (PCP)	Euphoria, nystagmus, ataxia, and emotional lability; hallucinations affecting body image that can result in panic reactions, disorientation, hypersalivation, and abusive language	8 d
Barbiturates	Sedation, pinpoint pupils, hypotension, bradycardia, hypothermia, hyporeflexia, as well as central nervous system and respiratory depression	1 d for short-acting agents; 2-3 wk for long-acting agents

**Table 2-1 • CLINICAL FEATURES OF SUBSTANCE ABUSE**

Treatment of life-threatening acute problems related to alcohol or drug use follows the **ABCs** of emergency care: manage the **A**irway, control **B**reathing, and assess the **C**irculation. Treatment then is directed at the offending agent (if known). After stabilization, a treatment plan is devised. For some, inpatient programs that disrupt drug use allow for continued outpatient therapy. For others, an intensive outpatient therapy program can be initiated to help develop a drug-free lifestyle. The expertise necessary to assist an adolescent through these changes is often beyond a general pediatrician's expertise. Assistance with this chronic problem by qualified health professionals in a developmentally appropriate setting can maximize outcome. Primary care providers can, however, assist families to find suitable community resources.

## COMPREHENSION QUESTIONS

- 2.1 A 14-year-old boy has ataxia. He is brought to the local emergency department, where he appears euphoric, emotionally labile, and a bit disoriented. He has nystagmus and hypersalivation. Many notice his abusive language. Which of the following agents is most likely responsible for his condition?
- A. Alcohol
  - B. Amphetamines
  - C. Barbiturates
  - D. Cocaine
  - E. Phencyclidine (PCP)
- 2.2 Parents bring their 16-year-old daughter for a “well-child” checkup. She looks normal on examination. As part of your routine care you plan a urinalysis. The father pulls you aside and asks you to secretly run a urine drug screen (UDS) on his daughter. Which of the following is the most appropriate course of action?
- A. Explore the reasons for the request with the parents and the adolescent, and perform a UDS with the adolescent's permission if the history warrants.
  - B. Perform the UDS as requested, but have the family and the girl return for the results.

- C. Perform the UDS in the manner requested.
  - D. Refer the adolescent to a psychiatrist for further evaluation.
  - E. Tell the family to bring the adolescent back for a UDS when she is exhibiting signs or symptoms such as euphoria or ataxia.
- 2.3 A previously healthy adolescent male has a 3-month history of increasing headaches, blurred vision, and personality changes. Previously he admitted to marijuana experimentation more than a year ago. On examination he is a healthy, athletic-appearing 17-year-old with decreased extraocular range of motion and left eye visual acuity. Which of the following is the best next step in his management?
- A. Acetaminophen (APAP) and ophthalmology referral
  - B. Glucose measurement
  - C. Neuroimaging
  - D. Trial of methysergide (Sansert) for migraine
  - E. Urine drug screen
- 2.4 An 11-year-old girl has dizziness, pupillary dilatation, nausea, fever, tachycardia, and facial flushing. She says she can “see” sound and “hear” colors. Which of the following agents is responsible for this?
- A. Alcohol
  - B. Amphetamines
  - C. Ecstasy
  - D. Lysergic acid diethylamide (LSD)
  - E. PCP

## ANSWERS

- 2.1 E. PCP is associated with hyperactivity, hallucinations, abusive language, and nystagmus.
- 2.2 A. The adolescent’s permission should be obtained before drug testing. Testing “secretly” in this situation destroys the doctor-patient relationship.

- 2.3 C. Despite previous drug experimentation, his current neurologic symptoms and physical findings make drug use a less likely etiology. Evaluation for possible brain tumor is warranted.
- 2.4 D. LSD is associated with symptoms that begin 30 to 60 minutes after ingestion, peak 2 to 4 hours later, and resolve by 10 to 12 hours, including delusional ideation, body distortion, and paranoia. “Bad trips” result in the user becoming terrified or panicked; treatment usually is reassurance of the user in a controlled, safe environment.
- 

### CLINICAL PEARLS

- Cigarettes and alcohol are the most commonly used drugs in adolescence.
  - Marijuana is the most common illicit drug used in adolescence.
  - Substance abuse behaviors include drug dealing, prostitution, burglary, unprotected sex, automobile accidents, and physical violence.
  - Children at risk for drug use include those with significant behavior problems, learning difficulties, and impaired family functioning.
- 

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## CASE 3

A 36-year-old woman with little prenatal care delivers a 3900 g girl. The infant has decreased tone, upslanting palpebral fissures, epicanthal folds, redundant nuchal skin, fifth finger clinodactyly and brachydactyly, and a single transverse palmar crease.

- ▶ What is the most likely diagnosis?
- ▶ What is the next step in the evaluation?

### ANSWERS TO CASE 3: **Down Syndrome**

*Summary:* A newborn with dysmorphic features is born to a woman of advanced maternal age.

- **Most likely diagnosis:** Down syndrome (trisomy 21).
- **Next step in evaluation:** Infant chromosomal evaluation to confirm diagnosis, evaluation for other features of the syndrome, counseling, and family support.

## ANALYSIS

### *Objectives*

1. Know the physical features and problems associated with Down syndrome (DS) and other common trisomy conditions.
2. Understand the evaluation of a child with dysmorphic features consistent with DS.
3. Appreciate the counseling and support required by a family with a special-needs child.

### *Considerations*

This newborn has many DS features; confirmation is made with a chromosome evaluation. Upon identification of a child with possible DS, the health-care provider attempts to identify potentially life-threatening features, including cardiac or gastrointestinal (GI) anomalies. A thorough evaluation of the family's psychosocial environment is warranted; these children can be physically, emotionally, and financially challenging.

*Note:* This woman of advanced maternal age had limited prenatal care but was at high risk for pregnancy complications. Adequate care may have included a serum triple screen between the 15th and 20th weeks of pregnancy or a “genetic” ultrasound, which could have demonstrated a DS pattern. Further evaluation (amniocentesis for chromosomal analysis) then could have been offered.

## APPROACH TO:

### The Dysmorphic Child

## DEFINITIONS

**ADVANCED MATERNAL AGE:** The incidence of DS increases each year beyond the age of 35 years. At 35 years, the incidence is 1 in 378 live born infants, increasing to 1 in 106 by the age of 40 and to 1 in 11 by the age of 49 years.

**BRACHYDACTYLY:** Excessive shortening of hand and foot tubular bones resulting in a boxlike appearance.

**CLINODACTYLY:** Incurving of one of the digits (in DS the fifth digit curves toward the fourth digit due to midphalanx dysplasia).

**DYSMORPHIC CHILD:** A child with problems of generalized growth or body structure formation. These children can have a *syndrome* (a constellation of features from a common cause; ie, DS features caused by extra chromosome 21 material), an *association* (two or more features of unknown cause occurring together more commonly than expected; ie, **VATER** [Vertebral problems, Anal anomalies, Trachea problems, Esophageal abnormalities, and Radius or renal anomalies]), or a *sequence* (a single defect that leads to subsequent abnormalities; ie, Potter disease's lack of normal infant kidney function, causing reduced urine output, oligohydramnios,



and constraint deformities; common facial features include wide-set eyes, flattened palpebral fissures, prominent epicanthus, flattened nasal bridge, mandibular micrognathia, and large, low-set, cartilage-deficient ears).

**SERUM TRISOMY SCREENING:** Measurements of  $\alpha$ -fetoprotein (AFP), human chorionic gonadotropin (hCG), inhibin A, and estriol levels, usually performed at 15 to 20 weeks' gestation. These tests screen for a variety of genetic problems. Approximately 75% of DS babies and 80% to 90% of babies with neural tube defects will be identified by this testing.

## CLINICAL APPROACH

The first newborn evaluation occurs in the delivery room where attempts are made to successfully transition the infant from an intrauterine to an extrauterine environment; it focuses primarily on the **ABCs** of medicine—**A**irway, **B**reathing, and **C**irculation. The infant is then evaluated for possible abnormalities, including those that might fit into a pattern such as DS.

The prenatal history and course provide some important clues in the evaluation of a dysmorphic child. The parents' age (increased chromosomal abnormalities with increased maternal and sometimes paternal age), degree of fetal movement, maternal drug or teratogen exposure, family history of dysmorphia, and prenatal testing results, including triple screening and chorioamniotic or chorionic villus testing, may prove helpful. For instance, an older mother with a low AFP on her triple screen is at higher risk for having a DS child.

The physical examination is critical to the diagnosis of a dysmorphic child. For DS, a distinctive pattern can lead to a presumptive diagnosis; more than 90% of such children have features, including upslanting palpebral fissures, Brushfield spots (white or grey spots in the periphery of the iris), flat facial profile, small and rounded ears, excess nuchal skin, widespread nipples, pelvic dysplasia, joint hyperflexibility, fifth finger clinodactyly, a single transverse palmar (simian) crease, hypotonia, and a poor Moro reflex. Other features include brachycephaly (disproportionate shortness of the head), epicanthal folds, brachydactyly, wide spacing between first and second toes, and short stature.

In newborns with suspected DS, at least two potentially life-threatening conditions must be addressed. **Approximately 50% of DS infants have**



**cardiac defects—most commonly an endocardial cushion defect (60%), ventricular septal defect (VSD, 32%), and tetralogy of Fallot (6%).** A cardiology consultation and echocardiogram usually are indicated.

**Approximately 12% of DS infants have intestinal (usually duodenal) atresia,** some presenting with a history of polyhydramnios. All DS infants have hypotonia and sometimes slower feeding. Should an infant with presumed DS develop persistent vomiting after feeds (especially if bilious), an upper GI study likely will reveal the characteristic **“double-bubble” pattern of duodenal atresia;** surgical intervention is warranted.

Confirmation of DS requires chromosomal analysis. A complete, extra chromosome 21 (nondisjunction, ie, failure to segregate during meiosis) occurs in almost 95% of cases. Two percent of cases are caused by translocations (breakage and removal of a large DNA segment from one chromosome and attachment to a different one), and 3% are mosaics (more than one cell type; usually described as an abnormal cell percentage). Parents of a child with translocation-caused DS are evaluated for chromosomal aberrations; the recurrence risk can approach 100% in some cases.

Other newborn conditions associated with DS include hearing loss, strabismus, cataracts, nystagmus, and congenital hypothyroidism. Hearing is evaluated by the age of 3 months. An ophthalmologist evaluates the eyes by the age of 6 months, and thyroid function is assessed as part of the routine newborn screening program. Longer-term DS consequences include obesity, a higher leukemia risk, acquired hypothyroidism, atlantoaxial (cervical spine) instability, and premature aging with an increased risk of Alzheimer disease. All DS children are mentally retarded, but the intelligence quotients vary widely (mosaics can exhibit near-normal intelligence).

“Well-child care” takes on special meaning for DS children. In addition to providing routine care based on the American Academy of Pediatrics (AAP) guidelines for health supervision that apply to all children, the AAP has promulgated DS-specific guidelines (see [www.aap.org](http://www.aap.org)). Periodic objective thyroid, hearing, and vision screenings are focal points of concern. Equally important in successful DS management is appropriate psychosocial intervention. Proper home or environmental, educational, and vocational interventions can improve the DS child’s functioning level, facilitating his or her transition to adulthood. Providing family support and assisting with financial and medical support program applications are within the pediatrician’s realm.

## COMPREHENSION QUESTIONS

- 3.1 A small-for-gestational age infant is born to a 35-year-old woman. He has low-set and malformed ears, microcephaly, rocker-bottom feet, inguinal hernias, cleft lip and palate, and micrognathia. Chromosomal analysis is likely to reveal which of the following?
- A. Down syndrome (trisomy 21)
  - B. Edwards syndrome (trisomy 18)
  - C. Holt-Oram syndrome
  - D. Patau syndrome (trisomy 13)
  - E. Turner syndrome
- 3.2 A 15-day-old infant has respiratory distress. A quick observation suggests she has slight cyanosis, hepatosplenomegaly, and features consistent with DS. The cardiac examination demonstrates a loud first heart sound, a wide and fixed split second heart sound, a low-pitched, mid-diastolic murmur at the lower left sternal border, and a harsh apical holosystolic murmur in the mitral area. An echocardiogram is likely to demonstrate which of the following?
- A. Complete atrioventricular (AV) canal (endocardial cushion defect)
  - B. Hypoplastic left heart
  - C. Total anomalous venous return
  - D. Transposition of the great vessels
  - E. Tricuspid atresia
- 3.3 A small-for-gestational age, dysmorphic newborn infant has microcephaly and sloping forehead, cutis aplasia (missing portion of the skin and hair) of the scalp, polydactyly, microphthalmia, and omphalocele. Which of the following is the most likely diagnosis?
- A. Down syndrome (trisomy 21)
  - B. Edwards syndrome (trisomy 18)
  - C. Holt-Oram syndrome
  - D. Patau syndrome (trisomy 13)
  - E. Turner syndrome

- 3.4 The parents of an 8-year-old DS boy arrive for his annual well-child visit. He wants to participate in sports, including the Special Olympics. Until further evaluation can be completed, which of the following sports would you suggest as being safe?
- A. Diving
  - B. Football
  - C. Tennis
  - D. Tumbling
  - E. Wrestling

## ANSWERS

- 3.1 **B.** The child has trisomy 18. Other features include clenched hands with overlapping digits, small palpebral fissures, prominent occiput, short sternum, and cardiac defects (ventricular septal defect [VSD], atrial septal defect [ASD], patent ductus arteriosus [PDA], or coarctation of the aorta).
- 3.2 **A.** Although VSDs are common in DS, the most characteristic lesion is endocardial cushion defect (or atrioventricular [AV] canal defect). Slight cyanosis occurs because of the mixing of deoxygenated with oxygenated blood. In the AV canal, a range of defects involving the atrial septum, the ventricular septum, and one or both of the AV valves can be seen. A complete AV canal includes ASDs and VSDs with a common AV valve. A partial AV canal includes defects of the atrial septum and separate mitral and tricuspid valve orifices.
- 3.3 **D.** The appearance of cutis aplasia and polydactyly suggests trisomy 13. Other common features include holoprosencephaly (failure of growth of the forebrain), cleft lip or palate, postaxial polydactyly, flexed and overlapping fingers, coloboma, and cardiac defects (VSD, ASD, PDA, dextrocardia).
- 3.4 **C.** Until lateral cervical flexion–extension films confirm normal anatomy, contact sports and other activities that may result in forceful flexion of the neck should be avoided.
-

## CLINICAL PEARLS

- ▶ Down syndrome is the most common autosomal chromosome abnormality in live born infants, increasing in incidence with advanced maternal age.
  - ▶ The most common neonatal Down syndrome features are hypotonia with poor Moro reflex, flat faces, slanted palpebral fissures, laxity of joints, and excessive skin on the back of the neck.
  - ▶ Common problems associated with Down syndrome include cardiac defects and duodenal atresia.
  - ▶ Common features of trisomy 18 (Edwards) syndrome include weak cry, single umbilical artery, micrognathia with small mouth and high arched palate, clenched hand with overlapping of index finger over the third finger, simian crease, rocker-bottom feet, small pelvis, and short sternum.
  - ▶ Common features of trisomy 13 (Patau) syndrome include microcephaly and sloping forehead, deafness, scalp cutis aplasia, microphthalmia, coloboma, cardiac defect (especially ventricular septal defect), omphalocele, single umbilical artery, and hypersensitivity to agents containing atropine and pilocarpine.
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#### CASE 4

An 8-year-old boy presents to your clinic with a 3-day history of a “white coating” in his mouth. He denies having a sore throat, upper respiratory infection symptoms, gastrointestinal distress, change in appetite, or fever. His immunizations are current, he has no significant past medical history, and he has been developing normally per his mother. His weight, however, has fallen from the 25th percentile to the 5th percentile, and he has been hospitalized on three occasions in the last year with pneumonia or dehydration. His family history is remarkable only for maternal hepatitis C infection related to past intravenous (IV) drug use. The patient is afebrile today, but his examination is notable for severe gingivitis, bilateral cervical and axillary lymphadenopathy, exudates on his buccal mucosa, and hepatomegaly.

- What is the most likely diagnosis?
- What is the next step in evaluation?

## ANSWERS TO CASE 4: **Immunodeficiency**

*Summary:* A child with lymphadenopathy, organomegaly, weight loss, recurring infection, and oral lesions consistent with candidiasis.

- **Most likely diagnosis:** Immunodeficiency.
- **Next step in evaluation:** Gather additional history, including birth history, details of hospitalizations, dietary history, and patient and family histories of recurring or atypical infection. Consider testing for human immunodeficiency virus type 1 (HIV) and obtaining a complete blood count and comprehensive metabolic panel to assess cell counts, organ function, and nutritional status.

## ANALYSIS

### *Objectives*

1. Differentiate between primary and secondary immunodeficiency.
2. Understand selected etiologies of pediatric immunodeficiency.
3. Identify and manage pediatric HIV disease.

### *Considerations*

Recurring infections in this patient presenting with oral lesions, weight loss, and lymphadenopathy are concerning for immune system dysfunction. He may have a primary immunodeficiency due to an inheritable defect or an acquired (secondary) immunodeficiency related to HIV infection, malignancy, malnutrition, or other disorder. The maternal history of IV drug use makes pediatric HIV infection a strong likelihood, probably due to vertical transmission. Additional patient and family histories and selected initial laboratory tests will aid in diagnosis and help guide management.

APPROACH TO:

**The Child with Immunodeficiency**

## DEFINITIONS

**HIV DNA POLYMERASE CHAIN REACTION (PCR):** Primary assay to diagnose HIV infection in children under 18 months of age; detects HIV DNA in white blood cells; sensitivity and specificity greater than 95%; definitive exclusion of HIV with two negative assays after 1 month of age, assuming other immunologic studies are negative.

**HIV ANTIBODY ELISA:** Enzyme-linked immunosorbent assay (ELISA) screening for HIV immunoglobulin G (IgG); initially detectable 2 weeks to 6 months after exposure; sensitivity and specificity greater than 99%; false-positive rate less than 5 in 100,000 assays; false-negative results may occur after immunization or in hepatic disease, autoimmune disease, or advanced acquired immunodeficiency syndrome (AIDS).

**WESTERN BLOT:** Direct visualization of antibodies to virion proteins; can be used to confirm screening antibody assay; results can be indeterminate and require repeat testing.

**CD4 (T HELPER) CELL:** Essential for humoral (B-cell) and cellular (T-cell) immunity; binds to antigens presented by B cells, prompting antibody production, and to antigens presented by phagocytes, prompting lymphokine release; rendered dysfunctional in HIV infection.

## CLINICAL APPROACH

Evaluation of patients with recurring or atypical infection starts with a comprehensive history and systems review. Clinicians should inquire about perinatal history, growth and development, and past illnesses.

**Immunosuppression** is suggested by **failure to thrive (FTT) or atypical or difficult-to-eradicate infections** (recurring otitis refractory to multiple antimicrobials). Family history includes parental health concerns (unexplained weight loss, growth failure, or developmental delay in siblings) and recurring or atypical infection in immediate family members. A focused physical examination should then be performed to identify signs consistent with immunosuppression (wasting, generalized lymphadenopathy, and organomegaly).

**Primary** (syndromic) **immunodeficiency** is due to a genetic defect, either inherited or related to gene mutation; most are humoral in origin or characterized by both humoral and cellular dysfunction (severe combined

immunodeficiency). Other primary immunodeficiencies include phagocytic cell deficiency (chronic granulomatous disease due to defective macrophages) and complement deficiency (autoimmune disease or serious bacterial infection due to C2 deficiency). Patients with **secondary immunodeficiency** have normal immune function at birth, but subsequently develop an illness or metabolic abnormality that disrupts immune cell production or function. Conditions adversely affecting a patient's immune status include HIV infection, diabetes mellitus, malnutrition, hepatic disease, autoimmune disease (scleroderma), aging, and stress.

HIV is a global epidemic, with over 30 million people presumably infected worldwide. Unprotected sexual intercourse and needle sharing with IV drug use are known means of transmission. Prior to the mid-1980s, blood transfusion was also a risk factor. In the pediatric population, **HIV is typically acquired through vertical transmission**. Approximately 80% of pediatric cases involve intrapartum transfer, but HIV can also be acquired from infected secretions at delivery and from breast milk. It is important to know the HIV status of the pregnant female, so that antiretroviral therapy can be administered during pregnancy to decrease viral replication and diminish the potential for transfer to the neonate. An infected mother has a 25% chance of transmitting the virus to her newborn if antiretroviral therapy is not received during pregnancy. Zidovudine, when started by the mother during the second trimester and given to the baby through the age of 6 weeks, reduces the risk of HIV transmission to less than 10%.

HIV infection gives rise to **dysfunctional CD4 cells** resulting in overall immune system compromise and eventual opportunistic infection. Approximately 75% of pediatric patients who acquire HIV vertically follow a course similar to adults, with an extended period of disease inactivity; a patient will often remain asymptomatic for a decade or more until the CD4 count falls to a critical level. The remainder of patients progress rapidly during the first several months of life. Therefore, early determination of maternal HIV status and measures to decrease transmission are critical (avoiding breast-feeding, aggressive and appropriate neonatal HIV testing, early antiretroviral therapy).

Verification of HIV infection is made in the patient older than 18 months by performing an HIV antibody ELISA and subsequent Western blot for confirmation. Because of placental transfer of maternal antibodies, **diagnosis in younger patients is made by HIV DNA PCR testing**. Two assays are



performed on separate occasions to confirm the diagnosis. Subsequently, HIV RNA activity, CD4 cell count, and clinical findings are used to determine disease status. Centers for Disease Control and Prevention (CDC) classification of HIV status is based on the presence and severity of signs or symptoms and degree of immunosuppression. For example, a patient with *Pneumocystis jiroveci* (*carinii*) pneumonia (PCP), an AIDS-defining opportunistic infection, is classified “severe” disease (category C). Degree of immunosuppression is based on an age-adjusted CD4 count. For the patient in this case, a normal CD4 count would be more than or equal to 500 or 25%. Severe suppression is denoted by a CD4 count less than 200 or 15%.

Neonates born to HIV-positive women are tested at birth and at selected intervals through approximately 6 months of age. Traditionally, the exposed neonate receives 6 weeks of antiretroviral therapy in the form of zidovudine starting in the first few hours of life. **PCP prophylaxis** in the form of **trimethoprim (TMP)-sulfamethoxazole (SMX)** commences at approximately 6 weeks of age for HIV-positive infants. CD4 levels are followed in quarterly intervals in the patient who becomes HIV-positive. HIV RNA activity is followed and typically correlates with disease progression; RNA activity of more than 100,000 copies/mL has been associated with advanced progression and early death.

Treatment for HIV-positive patients is started early to diminish viral replication before mutation and antiretroviral resistance occur. The **three major classes of anti-retrovirals are nucleoside reverse transcriptase inhibitors** (didanosine, stavudine, zidovudine), **nonnucleoside reverse transcriptase inhibitors** (efavirenz, nevirapine), and **protease inhibitors** (indinavir, nelfinavir). Combination retroviral therapy in children has led to a marked decline in child mortality. Common adverse effects for all include headache, emesis, abdominal pain, and diarrhea. Osteopenia and drug rash can also be seen. Possible other abnormalities include anemia, neutropenia, elevated transaminases, hyperglycemia, and hyperlipidemia.

The current pediatric antiretroviral therapy recommendation consists of three drugs: two nucleoside reverse transcriptase inhibitors and one protease inhibitor. An existing treatment regimen is altered when toxicity becomes an issue or disease progression occurs. Ultimately, HIV treatment requires a multidisciplinary approach with input from nutritionists, social workers, and pediatric HIV and mental health specialists. In addition to periodic monitoring of viral activity and prophylaxis against opportunistic infection, close

monitoring of growth, development, and emotional health is important in pediatric HIV disease management. **Immunizations** should be kept current, with all vaccines administered per the recommended pediatric schedule, excluding live vaccines such as measles-mumps-rubella (MMR) and varicella for symptomatic HIV-infected children with a CD4 count less than 15%.

## COMPREHENSION QUESTIONS

- 4.1 A 15-year-old adolescent girl has a 1-month history of urinary frequency without dysuria and the complaint of a recent onset of an itchy rash beneath both breasts. She has been gaining weight over the past year and regularly complains of fatigue. She is afebrile with a weight greater than the 99th percentile and has an erythematous, macular rash beneath both breasts characterized by satellite lesions. Urinalysis is significant for 2+ glucosuria, but no pyuria. Which of the following is the best next step in your evaluation?
- A. HIV RNA level
  - B. Hemoglobin A1c
  - C. CD4 cell count
  - D. Herpes simplex virus-1 IgG
  - E. Thyroid stimulating hormone
- 4.2 A mother notes her 6-week-old son's umbilical cord is still attached. His activity and intake are normal; he has had no illness or fever. Delivery was at term without problems. His examination is notable for a cord without evidence of separation and a shallow, 0.5-cm ulceration at the occiput without discharge or surrounding erythema. Mother declares that the "sore," caused by a scalp probe, has been slowly healing since birth and was deemed unremarkable at his 2-week checkup. Which of the following is consistent with this child's likely diagnosis?
- A. Defective humoral response
  - B. Functional leukocyte adherence glycoproteins
  - C. Marked neutrophilia
  - D. Normal wound healing

E. Purulent abscess formation

4.3 A 6-month-old girl is seen after an emergency room visit for decreased intake, emesis, and watery diarrhea for the past 3 days. She was diagnosed yesterday with “stomach flu” and given IV fluids. She is doing better today with improved intake and resolution of her emesis and diarrhea. The father is concerned about her thrush since birth (despite multiple courses of an oral antifungal), and that she has been hospitalized twice for pneumonia over the past 4 months. Her weight has dropped from the 50th percentile on her 4-month visit to the 5th percentile today. She has no findings consistent with dehydration, but she does appear to have some extremity muscle wasting. Her examination is remarkable for buccal mucosal exudates and hyperactive bowel sounds. Vital signs and the remainder of her examination are normal. You suspect severe combined immunodeficiency (SCID). Which of the following is consistent with the diagnosis?

- A. Autosomal dominant inheritance
- B. Persistent lymphocytosis
- C. Defective cellular immunity
- D. Normal vaccine immune response
- E. No curative therapy

4.4 You are called urgently to examine a term, 2-hour-old newborn with temperature instability, difficulty with feeding, and a suspected seizure. He has atypical facies (wide-set eyes, a prominent nose, and a small mandible), a cleft palate, and a holosystolic murmur. A chest radiograph reveals a boot-shaped heart. Which of the following is consistent with this infant’s likely diagnosis?

- A. Hypercalcemia
- B. Chromosomal duplication
- C. Parathyroid hyperplasia
- D. Hypophosphatemia
- E. Thymic aplasia

## ANSWERS

- 4.1 B. The obese adolescent in this case has findings of diabetes mellitus. An elevated hemoglobin A1c (glycosylated hemoglobin) is a good diagnostic tool for diabetes. This patient's cutaneous candidiasis is likely an indication of secondary immunosuppression related to hyperglycemia. In diabetes, hyperglycemia promotes neutrophil dysfunction, and circulatory insufficiency contributes to ineffective neutrophil chemotaxis during infection. HIV infection is possible and testing might be reasonable, but this scenario is most consistent with hyperglycemia.
- 4.2 C. You suspect leukocyte adhesion deficiency (LAD) as the etiology of this child's problem. LAD is an inheritable disorder of leukocyte chemotaxis and adherence characterized by recurring sinopulmonary, oropharyngeal, and cutaneous infections with delayed wound healing. Neutrophilia is common with WBC counts typically more than 50,000 cells/mm<sup>3</sup>. Severe, life-threatening infection is possible with *Staphylococcus* species, *Enterobacteriaceae*, and *Candida* species. Good skin and oral hygiene are important; broad-spectrum antimicrobials and surgical debridement are early considerations with infection.
- 4.3 C. Severe combined immunodeficiency (SCID) is an autosomal recessive or X-linked disorder of both humoral and cellular immunity. Serum immunoglobulins and T cells are often markedly diminished or absent. Thymic dysgenesis is also seen. Recurring cutaneous, gastrointestinal, or pulmonary infections occur with opportunistic organisms such as cytomegalovirus (CMV) and *Pneumocystis pneumonia* (PCP). Death typically occurs in the first 12 to 24 months of life unless bone marrow transplantation is performed.
- 4.4 E. The child in the question has typical features of DiGeorge syndrome, caused by a 22q11 microdeletion. This syndromic immunodeficiency is characterized by decreased T-cell production and recurring infection. Findings include characteristic facies and velocardiofacial defects such as ventricular septal defect and tetralogy of Fallot. Thymic or parathyroid dysgenesis can occur, accompanied by hypocalcemia and seizures. Developmental and speech delay are common in older patients.

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## CLINICAL PEARLS

- Primary immunodeficiency is an inheritable disorder characterized by weakened immunity and recurring, serious infection early in life.
  - A variety of illnesses can provoke secondary immunodeficiency; malignancy, malnutrition, hepatic disease, and HIV infection are known to adversely influence both humoral and cellular immunity.
  - Pediatric HIV disease can be deterred by appropriate testing and treatment of pregnant females and judicious antiretroviral prophylaxis in the exposed neonate. Exposed patients should be closely followed by clinicians and a team approach used in the management of active disease.
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A 13-year-old boy arrives for routine care. His mother reports that he seems to be much more immature and insecure than her older son was at the same age. His school performance is below average, and this year he has begun to receive special education for language-based classes. On physical examination you note that he is at the 95th percentile for height-age, his extremities are longer than expected, and he is embarrassed by his gynecomastia. His physical examination shows that he has Tanner stage 1 sexual development with small gonads.

- ▶ What is the most likely diagnosis?
- ▶ What is the best test to diagnose this condition?

### ANSWERS TO CASE 5: **Klinefelter Syndrome**

*Summary:* A tall, immature, and insecure 13-year-old boy with hypogonadism, long limbs, gynecomastia, and developmental delay.

- **Most likely diagnosis:** Klinefelter syndrome, a trisomy syndrome of nondisjunction affecting approximately 1 in 600 to 800 male infants.
- **Best diagnostic test:** Chromosomal analysis.

## ANALYSIS

### *Objectives*

1. Understand the signs and symptoms of Klinefelter syndrome.
2. Appreciate the variety of causes of childhood mental retardation (MR).
3. Learn the signs and symptoms of syndromes involving missing or duplicate sex chromosomes.

### *Considerations*

This child's mother has identified this adolescent's development and behavior to be different from her other children. The school recently has identified his need for special education, especially in the language-based classes. A thorough history (including all school performance and behavioral problems) and physical examination can provide diagnostic clues. The etiology of his

condition impacts his psychosocial outcome, his future medical therapy, and his parents, family planning decisions.

APPROACH TO:

**Klinefelter Syndrome**

## DEFINITIONS

**KLINEFELTER SYNDROME:** A specific syndrome associated with behavioral problems (immaturity, insecurity), developmental delay (speech, language, lower IQ), and physical findings (gynecomastia, hypogonadism, long limbs) caused by an extra X chromosome in boys and men.

**MENTAL RETARDATION (MR):** A clinically and socially important impairment of measured intelligence and adaptive behavior that is diagnosed before 18 years of age.

## CLINICAL APPROACH

Causes of MR include **preconceptual and early embryonic disruptions** (teratogens, chromosomal abnormalities, placental dysfunction, congenital central nervous system [CNS] malformations); **fetal brain insults** (infections, toxins, placental problems); **perinatal difficulties** (prematurity, metabolic disorders, infections); **postnatal brain injuries** (infections, trauma, metabolic disorders, toxins, poor nutrition); and miscellaneous **postnatal family difficulties** (poverty, poor caregiver-child interaction, parental mental illness). A category of “unknown etiology” includes children with MR who do not fit into the above categories.

The history of a child with possible MR includes an evaluation of the child’s psychosocial skills and a review of school reports. The ultimate diagnosis may require formal testing to determine if the IQ falls below some set point, such as 80. A determination of whether formal testing should be performed is based on physical examination findings, developmental and school histories, and concerns of the family and teachers. Males with Klinefelter syndrome often have developmental delay, especially in verbal cognitive areas where they underachieve in reading, spelling, and mathematics; their full IQ may be normal, but their verbal IQ usually is

somewhat decreased. In variants with multiple X chromosomes, the incidence and severity of MR increases. **Boys with Klinefelter syndrome often go unidentified until puberty because of the subtleness of the clinical findings. The diagnosis should be considered for all boys (regardless of age) who have been identified as having mental retardation, or psychosocial, school, or adjustment problems.**

Physical findings to be considered in patients with nonspecific MR include the size of the occiput, unusual hair color or distribution, distinctive eyes, malformed ears or nose, and abnormalities in jaw size, mouth shape, or palate height. The hands and feet may have short metacarpals or metatarsals, overlapping or supernumerary digits, and abnormal creases or nails. The skin may have café au lait spots or depigmented nevi, and the genitalia may be abnormally sized or ambiguous. Patients with MR caused by Klinefelter syndrome typically are tall, slim, and thin with long extremities (see [Figure 5-1](#)). Their testes and sometimes the phallus are small for age, but these latter findings may not become apparent until puberty. As adults, males with Klinefelter syndrome develop gynecomastia, sparse facial hair, and azoospermia. The incidence of breast cancer (as well as some hematologic cancers) is elevated in Klinefelter syndrome.





**Figure 5-1.** Klinefelter syndrome (XXY) in a 20-year-old man. Note relatively increased lower/upper body segment ratio, gynecomastia, small penis, and sparse body hair with a female pubic hair pattern. (Reproduced, with permission, from Gardner DG, Shoback D. *Greenspan's Basic & Clinical Endocrinology*, 9th ed., New York: McGraw-Hill, 2011. Figure 12-7.)

Laboratory testing of a child with MR is based on the clinical findings and developmental milestones. A chromosomal analysis is often included in the evaluation of a child with mental retardation; for Klinefelter syndrome such an analysis will demonstrate the extra X-chromosome material. Other MR testing may include urine and serum amino and organic acids, serum levels of various compounds including ammonia, lead, zinc, and copper, and serum titers for congenital infections. Radiologic evaluation may include cranial computed tomography (CT), magnetic resonance imaging (MRI), or electroencephalogram (EEG).

Management of children with MR includes specialized educational services, early childhood interventions, social services, vocational training, and psychiatric interventions. Further interventions for children with specific underlying etiologies may include diet modification, genetic counseling, or reviewing the natural disease course with the family.

## COMPREHENSION QUESTIONS

- 5.1 An institutionalized male juvenile delinquent upon close examination has severe nodulocystic acne, mild pectus excavatum, large teeth, prominent glabella, and relatively long face and fingers. His family says he has poor fine motor skills (such as penmanship), an explosive temper, and a low-normal IQ. What is the most likely diagnosis?
- A. Fragile X syndrome
  - B. Klinefelter syndrome (XXY)
  - C. Turner syndrome (XO)
  - D. XXX syndrome
  - E. XYY male
- 5.2 A tall, thin 14-year-old adolescent male has no signs of puberty. He was delayed in his speech development and always has done less well in school than his siblings. He is shy, and teachers report that his activity is immature. Physical examination reveals breast development and long limbs with a decreased upper segment–lower segment ratio. He has small testes and phallus. What is the most likely diagnosis?
- A. Fragile X syndrome
  - B. Klinefelter syndrome (XXY)
  - C. Turner syndrome (XO)
  - D. XXX syndrome
  - E. XYY male
- 5.3 A 15-year-old adolescent girl with primary amenorrhea is noted to be well below the fifth percentile for height. She has hypertension, a low posterior hairline, prominent and low-set ears, and excessive nuchal skin. What is the most likely diagnosis?

- A. Fragile X syndrome
- B. Klinefelter syndrome (XXY)
- C. Turner syndrome (XO)
- D. XXX syndrome
- E. XYY phenotypic female

5.4 A 7-year-old boy with MR was born at home at 26 weeks' gestation to a 28-year-old mother who had received no prenatal care. An evaluation is likely to suggest his MR is related to which of the following?

- A. Brain tumor
- B. Chromosomal aberration
- C. Complications of prematurity
- D. Congenital infection with cytomegalovirus
- E. Elevated serum lead levels

## ANSWERS

5.1 E. XYY-affected males often have explosive tempers. Other findings include long and asymmetrical ears, increased length versus breadth for the hands, feet, and cranium, and mild pectus excavatum. By the age of 5 to 6 years, they tend to be taller than their peers and begin displaying aggressive or defiant behavior.

5.2 B. With Klinefelter syndrome, testosterone replacement allows for more normal adolescent male development, although azoospermia is the rule; the breast cancer incidence approaches that of women.

5.3 C. Turner syndrome also includes widely spaced nipples and broad chest; cubitus valgus (increased carrying angle of arms); edema of the hands and feet in the newborn period; congenital heart disease (coarctation of the aorta or bicuspid aortic valve); horseshoe kidney; short fourth metacarpal and metatarsal; hypothyroidism; and decreased hearing. Mental development usually is normal.

5.4 C. Prematurity, especially when earlier than 28 weeks' gestation, is associated with complications (such as intraventricular hemorrhage) that

can result in developmental delay and low IQ.

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### CLINICAL PEARLS

- Males with Klinefelter syndrome (XXY) have mild mental delay, eunuchoid habitus, gynecomastia, long arms and legs, and hypogonadism.
  - XYY males have explosive (often antisocial) behavior, weakness with poor fine motor control, accelerated growth in mid-childhood, large teeth, prominent glabella and asymmetrical ears, and severe acne at puberty.
  - Girls with Turner syndrome (45, XO) have short stature, amenorrhea, excessive nuchal skin, low posterior hairline, broad chests with widely spaced nipples, cubitus valgus, and coarctation of the aorta. Hypertension is common, possibly due to renal abnormalities (horseshoe kidney).
  - Fragile X syndrome, the most common form of inherited mental retardation, is seen primarily in boys and can be diagnosed in patients with mental retardation (particularly boys) who have macrocephaly, long face, high arched palate, large ears, and macroorchidism after puberty.
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## CASE 6

A 6-month-old child arrives for a well-child examination. His family recently moved to the United States from Turkey. His medical and family histories are unremarkable except that his sole source of nutrition is goat's milk. He appears to be healthy on examination.

- What hematologic problem is most likely to develop?
- What nonhematologic concerns are considered in an infant fed on goat's milk?

## ANSWERS TO CASE 6: **Megaloblastic Anemia**

*Summary:* This is a 6-month-old child exclusively fed on goat's milk.

- **Likely complication:** Megaloblastic anemia from folate or B<sub>12</sub> deficiency.
- **Other concerns:** Brucellosis if milk is unpasteurized.

## ANALYSIS

### *Objectives*

1. Appreciate the benefits of breast-feeding.
2. Know the nutritional supplements recommended for breast-feeding mothers.
3. Understand the special needs of infants and toddlers fed on goat's milk or vegan diets.
4. Appreciate the clinical syndromes resulting from vitamin excesses and deficiencies.

### *Considerations*

A variety of feeding regimens exist for infants and toddlers—breast-feeding, goat's milk, other types of nonformula milk, and commercial or handmade foods. Health-care providers can educate parents about the benefits and potential dangers of various diet choices.

APPROACH TO:

**Infant Nutrition**

## DEFINITIONS

**LACTOVEGETARIAN:** Diet devoid of animal products but includes milk.

**OMNIVORE:** Diet includes both animal and vegetable products.

**OVOVEGETARIAN:** Diet devoid of animal products but includes eggs.

**VEGAN:** Vegetarian diet devoid of all animal products.

## CLINICAL APPROACH

Infant formulas containing goat's milk are not routinely available in the United States, but they are available elsewhere. Goat's milk has lower sodium levels but more potassium, chloride, linoleic acid, and arachidonic acid than does cow's milk. It is low in vitamin D, iron, folate, and vitamin B<sub>12</sub>; infants receiving **goat's milk** as a primary nutrition source are given **folate** and **vitamin B<sub>12</sub>** (to prevent megaloblastic anemia) and iron (to prevent iron deficiency anemia). **Goat's milk** is boiled before ingestion; goats are particularly susceptible to **brucellosis**.

Breast milk is considered the ideal human infant food because it contains complete nutrition (with the possible exception of vitamin D and fluoride); iron levels are low but highly bioavailable and do not require supplementation until 4 to 6 months of age. In addition, it has antimicrobial properties and offers psychological advantages to mothers and infants. In developing countries, it is associated with lower infant morbidity and mortality, not only due to a reduction in diarrhea associated with contaminated water used in formula preparation but also because it contains **high concentrations of immunoglobulin A (IgA)**, which reduces viruses and bacteria intestinal wall adherence, and macrophages, which inhibit *Escherichia coli* growth. **Disadvantages** include potential **HIV** (and other virus) transmission, occasional **jaundice exacerbation** due to increased unconjugated bilirubinemia levels (resolved with a 12- to 24-hour breast-feeding interruption), and its association with **low vitamin K** levels, contributing to hemorrhagic disease of the newborn (prevented by vitamin K administration at birth).

Formula feeding is substituted for breast-feeding for a variety of reasons. Commercial formula manufacturers strive to provide products similar to human milk. Infant growth rates with cow's milk formula are similar to those in infants receiving breast milk. Improved sterilization procedures and refrigeration in developed and developing countries have reduced to some degree the gastrointestinal (GI) infections noted with formula feedings.

Formulas are available for special-needs infants. Infants with phenylketonuria require formulas low in phenylalanine, and those unable to digest protein require nitrogen in the form of amino acid mixtures.

Vegan diets supply all necessary nutrients if a variety of vegetables is selected. Some evidence suggests that high-fiber vegetarian diets lead to faster gastrointestinal transit time, resulting in reduced serum cholesterol levels, less diverticulitis, and a lower appendicitis incidence. Breast-feeding vegan mothers are given vitamin B<sub>12</sub> to prevent the infant's developing methylmalonic acidemia (an amino acid metabolism disorder involving a defect in the conversion of methylmalonyl-coenzyme A [CoA] to succinyl-CoA); patients can present with failure to thrive, seizure, encephalopathy, stroke, or other neurologic manifestations. Toddlers on a vegan diet are given vitamin B<sub>12</sub> and, because of the high fiber content and rapid gastrointestinal transit time, are given trace minerals that can be depleted.

Vitamin deficiencies and excesses can result in a variety of clinical syndromes. Although rare, these syndromes usually can be averted with appropriate nutrition ([Table 6-1](#)).



	Deficiency	Excess
Vitamin A	Night blindness, xerophthalmia, keratomalacia, conjunctivitis, poor growth, impaired resistance to infection, abnormal tooth enamel development	Increased intracranial pressure (ICP), anorexia, carotenemia, hyperostosis (pain and swelling of long bones), alopecia, hepatomegaly, poor growth
Vitamin D	Rickets (with elevated serum phosphatase levels appearing before bone deformities), osteomalacia, infantile tetany	Hypercalcemia, azotemia, poor growth, nausea and vomiting, diarrhea, calcinosis of a variety of tissues including kidney, heart, bronchi, stomach
Vitamin E	Hemolytic anemia in premature infants	Unknown
Ascorbic acid (vitamin C)	Scurvy and poor wound healing	Predisposition to kidney stones

Thiamine (vitamin B <sub>1</sub> )	Beriberi (neuritis, edema, cardiac failure), hoarseness, anorexia, restlessness, aphonia	Unknown
Riboflavin (vitamin B <sub>2</sub> )	Photophobia, cheilosis, glossitis, corneal vascularization, poor growth	Unknown
Niacin	Pellagra (dementia, dermatitis, diarrhea)	Nicotinic acid causes flushing, pruritus
Pyridoxine (vitamin B <sub>6</sub> )	In infants, irritability, convulsions, anemia; in older patients (on isoniazid [INH]), dermatitis, glossitis, cheilosis, peripheral neuritis	Sensory neuropathy

Folate	Megaloblastic anemia, glossitis, pharyngeal ulcers, impaired cellular immunity	Usually none, although extremely high levels can cause stomach problems, sleep disturbance, skin reactions, and seizures
Cobalamin (vitamin B <sub>12</sub> )	Pernicious anemia, neurologic deterioration, methylmalonic acidemia	Unknown
Pantothenic acid	Rarely depression, hypotension, muscle weakness, abdominal pain	Unknown
Biotin	Dermatitis, seborrhea, anorexia, muscle pain, pallor, alopecia	Unknown
Vitamin K	Hemorrhagic manifestations.	Water-soluble forms can cause hyperbilirubinemia

**Table 6-1 • EFFECTS OF VITAMIN AND MINERAL DEFICIENCY OR EXCESS**

## COMPREHENSION QUESTIONS

**6.1** A 2-day-old infant has significant nasal and rectal bleeding. The pregnancy was without complications; he was delivered by a midwife at home. His Apgar scores were 9 at 1 minute and 9 at 5 minutes. He has breast-fed well and has not required a health-care professional visit since birth. Which of the following vitamin deficiencies might explain his condition?

A. Vitamin A

B. Vitamin B<sub>1</sub>

C. Vitamin C

D. Vitamin D

E. Vitamin K

6.2 A 6-month-old infant has been growing poorly. His parents have changed his formula three times without success. His examination is remarkable for a pale, emaciated child with little subcutaneous fat and anterior fontanelle fullness. His laboratory test results are notable for a hemolytic anemia and prolonged bleeding times. Which of the following is the most appropriate next step?

A. Gather urine for pH and electrolytes.

B. Measure serum factor IX levels.

C. Measure serum immunoglobulins.

D. Obtain a sweat chloride concentration.

E. Perform a hemoglobin electrophoresis.

6.3 An exclusively breast-fed infant with poor routine care is switched at 6 months of age to whole milk and table foods. Screening laboratories at 9 months of age demonstrate the hemoglobin and hematocrit to be 8 mg/dL and 25%, respectively, and the lead level to be less than 2 µg/dL. A follow-up complete blood count (CBC) 2 weeks later shows the hemoglobin to be at 7.8 mg/dL, the hematocrit 25%, the mean corpuscular volume (MCV) 62%, the platelet count to be 750,000/mm<sup>3</sup>, and a reticulocyte count of 1%. Which of the following would be the next step in the management of this child?

A. Order a hemoglobin electrophoresis.

B. Obtain a bone marrow aspiration.

C. Initiate iron supplementation.

D. Refer to a pediatric hematologist.

E. Initiate soybean-based formula.

6.4 A 3-week-old is admitted for failure to thrive, diarrhea, and a septic appearance. He does well on intravenous fluids; when begun on routine infant formula with iron, his symptoms return. It is Saturday and the state

health department laboratory is closed. You should begin feeds with which of the following?

- A. Amino acid-based formula (Nutramigen or Pregestimil)
- B. Low-phenylalanine formula (Lofenalac or Phenex-1)
- C. Low-iron, routine infant formula (Similac with low iron or Enfamil with low iron)
- D. Low-isoleucine, low-leucine, low-valine infant formula (Ketonex-1 or MSUD 1)
- E. Soy-based formula (Isomil or ProSobee)

## ANSWERS

- 6.1 E. Newborn infants have a relative vitamin K deficiency, especially if they are breast-fed; most infants are given vitamin K at birth to prevent deficiency-related bleeding complications.
- 6.2 D. The patient appears to have failure to thrive, with deficiencies of vitamin K (bleeding problems), vitamin A (fontanelle fullness), and vitamin E (hemolytic anemia). Cystic fibrosis (associated with vitamin malabsorption) would explain the condition.
- 6.3 C. The child in the question most likely did not get iron (or vitamin D) supplementation in the first 6 months of life while exclusively breast-feeding, and was switched to whole milk (low in iron) and to table foods (not supplemented with iron as are baby foods) at too young an age. All of the laboratory data are consistent with iron deficiency anemia; iron supplementation in this child with a resultant brisk erythrocyte response is both diagnostic and therapeutic. Failure of the child to respond to the iron therapy would require further evaluation.
- 6.4 E. This patient appears to have galactosemia; uridyl transferase deficiency is the cause, and the condition results in features of jaundice, hepatosplenomegaly, vomiting, hypoglycemia, seizures, lethargy, irritability, poor feeding and failure to thrive, aminoaciduria, liver failure, mental retardation, and an increased risk of *E coli* sepsis. Children with galactosemia are managed with a lactose-free formula. The low-phenylalanine formulas are for infants with phenylketonuria; low-

iron formulas serve no purpose other than causing iron deficiency anemia; the low-isoleucine, low-leucine, low-valine infant formulas are useful for patients with maple syrup urine disease (MSUD); and the amino acid-based formulas are excellent for children with malabsorption syndromes.

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## CLINICAL PEARLS

- ▶ Breast-feeding is associated with lower morbidity and mortality (especially in developing countries) mostly because of a reduction in enteric pathogens and diarrhea associated with contaminated water used in formula preparation.
  - ▶ Breast-feeding provides all the nutrients necessary for infant growth with the possible exceptions of vitamin D and fluoride, which usually are supplemented.
  - ▶ A breast-feeding vegan should supplement her infant's or toddler's diet with vitamin B<sub>12</sub> to prevent methylmalonic acidemia and trace minerals.
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## CASE 7

An 8-month-old child has a 24-hour history of increased crying when she moves her right leg. She has a prominent bulge over the mid-right thigh where she had received an immunization the previous day. She has not had fever or change in appetite, and she seems upset only when the leg is disturbed. The child underwent a failed Kasai procedure for biliary atresia and is awaiting a liver transplant. A radiograph of the leg demonstrates a mid-shaft fracture and poor mineralization.

- What is the mechanism for this condition?
- What are the best diagnostic tests to diagnose this condition?

## ANSWERS TO CASE 7: **Rickets**

*Summary:* An 8-month-old child with a chronic medical condition, including biliary atresia, poor bone mineralization, and a fracture.



- **Mechanism:** Malabsorption of vitamin D (among other fat-soluble vitamins) due to lack of intestinal secretion of bile salts, resulting in rickets.
- **Best diagnostic tests:** Serum 25(OH)D, calcium, phosphorus, and alkaline phosphatase levels. Radiographs demonstrate poor bone mineralization.

## ANALYSIS

### *Objectives*

1. Become familiar with the clinical presentation of rickets.
2. Understand the pathophysiology behind nutritional and nonnutritional rickets.
3. Appreciate some of the other causes of childhood fractures.

### *Considerations*

This child has biliary atresia and underwent a failed Kasai procedure. Metabolic aberrations are expected while this child awaits liver transplantation. A review of her medications and compliance in receiving them is warranted. Because of the brittle nature of her bones, her leg was fractured while receiving immunizations.

### APPROACH TO:

#### **The Child with Possible Rickets**

## DEFINITIONS

**BILIARY ATRESIA:** A congenital condition affecting approximately 1 in 16,000 live births in which the liver's bile ducts become blocked and fibrotic, resulting in reduced bile flow into the bowel.

**GENU VALGUM:** "Knock" knees.

**GENU VARUM:** "Bowed" legs.

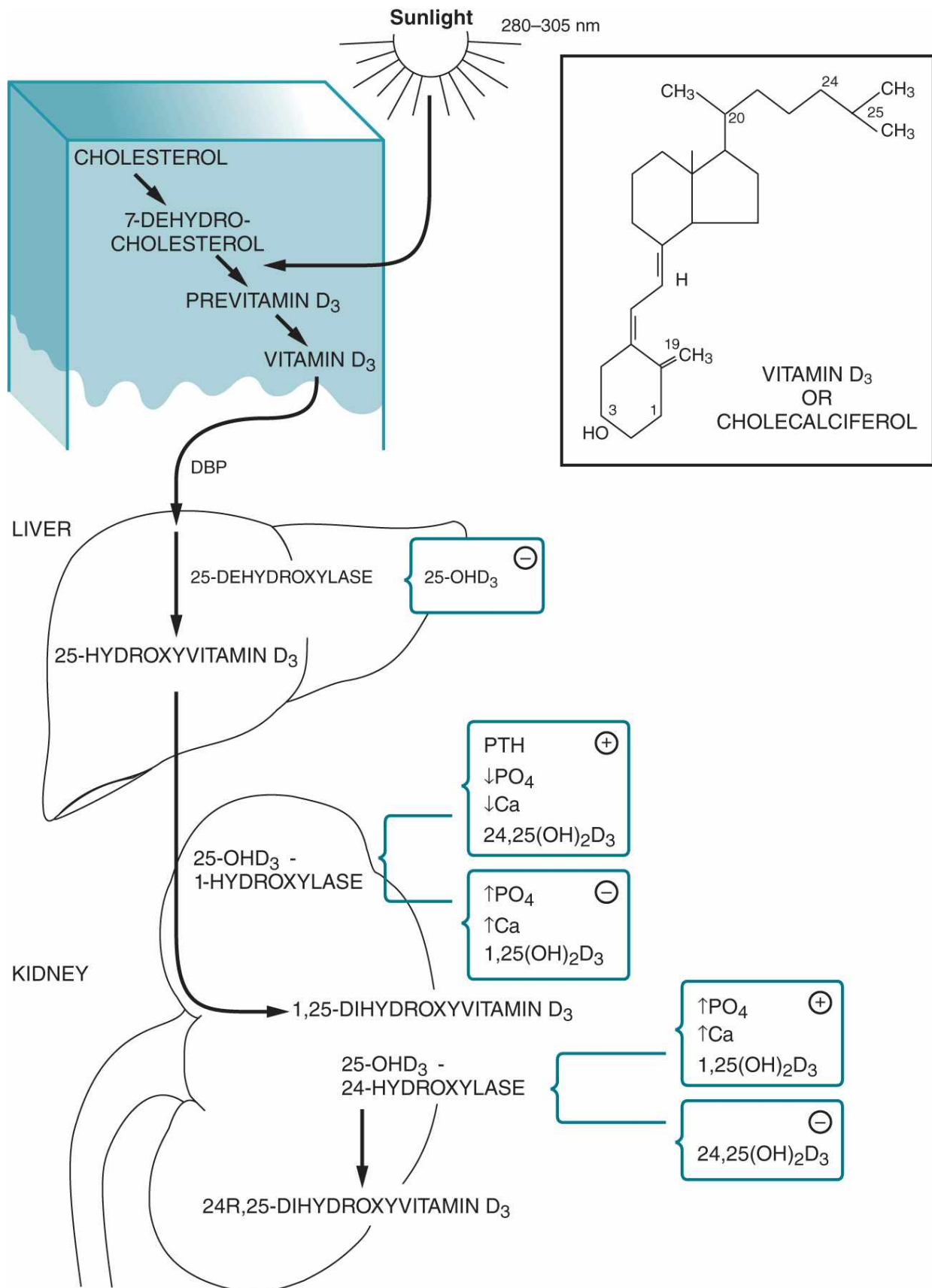
**KASAI PROCEDURE:** An operative procedure in which a bowel loop forms a duct to allow bile to drain from a liver with biliary atresia.

**RICKETS:** Poor mineralization of growing bone or of osteoid tissue.

## CLINICAL APPROACH

A patient with **liver failure** has **poor bile salt secretion**, resulting in **poor fat-soluble vitamin absorption**, including **vitamin D**. The **poor vitamin D absorption** causes low serum 25(OH)D, occasionally **reduced serum calcium levels**, markedly **elevated serum alkaline phosphatase**, **poor bone mineralization**, and an increased risk of fractures. Children with liver failure and ascites are treated with loop diuretics, which often cause urinary calcium losses. Treatment, aimed at restoring normal bone mineralization, consists of high vitamin D doses and calcium supplementation.

**Nutritional rickets**, resulting from **inadequate dietary vitamin D** or a lack of sunlight exposure ([Figure 7-1](#)), is rare in industrialized countries in healthy children. It is occasionally seen in dark-skinned infants who do not receive vitamin D supplementation or in breast-fed infants not exposed to sunlight. More common causes of rickets are liver or renal failure and a variety of biochemical abnormalities in calcium or phosphorus metabolism ([Table 7-1](#)).



**Figure 7-1. Vitamin D metabolism.**

	Serum Calcium	Phosphorus	Serum Alkaline Phosphatase	Urine Amino Acids	Comments
Calcium deficiency with secondary hyperparathyroidism [vitamin D deficiency or low 25(OH)D without stimulation of 1,25(OH) <sub>2</sub> D production]					
Lack of vitamin D (lack of exposure to sunlight; dietary deficiency vitamin D, congenital)	N or ↓	↓	↑	↑	Unusual except in dark-skinned infants without vitamin D supplementation, or in exclusively breast-fed infants without exposure to sunlight
Malabsorption of vitamin D	N or ↓	↓	↑	↑	Such as in celiac disease, cystic fibrosis, or steatorrhea
Hepatic disease	N or ↓	↓	↑	↑	See discussion of case
Anticonvulsive drugs	N or ↓	↓	↑	↑	Usually phenobarbital and phenytoin; patients have reduced 25(OH)D levels, possibly as a result of increased cytochrome P450 activity; treatment is with vitamin D <sub>2</sub> and adequate dietary calcium

Renal osteodystrophy	N or ↓	↓	↑	Variable	Hypophosphaturia results in hypocalcemia that then stimulates parathyroid secretion and enhanced bone turnover. Additionally, diminished conversion of 25(OH)D to 1,25(OH) <sub>2</sub> D occurs as renal damage progresses
Vitamin D-dependent type I	↓	N or ↓	↑	↑	Autosomal recessive; believed to be reduced activity of 25 (OH)D <sub>1</sub> α-hydroxylase; responds to massive doses of vitamin D2 or low-dose 1,25(OH) <sub>2</sub> D
Phosphate deficiency without secondary hyperparathyroidism					
Genetic primary hypophosphatemia	N	↓	↑	N	X-linked dominant; most common form of nonnutritional rickets (see text)

Fanconi syndrome	N	↓	↑	↑	Includes cystinosis, tyrosinosis, Lowe syndrome, and acquired forms. Cystinosis and tyrosinosis are autosomal recessive, Lowe syndrome X-linked recessive
Renal tubular acidosis, type II (proximal)	N	↓	↑	N	Bicarbonaturia, hyperkaluria, hypercalciuria, hypophosphatemia, and phosphaturia are common. Rickets may result from leaching of bone calcium bicarbonate in an attempt to buffer retained hydrogen ions seen in this condition
Oncogenic hypophosphatemia	N	↓	↑	Usually N	Caused by tumor secretion of a phosphate-regulating gene product (PEX), which results in phosphaturia and impaired conversion of 25(OH)D to 1,25(OH) <sub>2</sub> D. The tumors are often hard to detect but are found in the small bones of the hands and feet, abdominal sheath, nasal antrum, and pharynx. Resolution occurs after tumor removal
Phosphate deficiency or malabsorption	N	↓	↑	N	Caused by parenteral hyperalimentation or low-phosphate intake
End-organ resistance to 1,25(OH) <sub>2</sub> D <sub>3</sub>					
Vitamin D-dependent type II	↓	↓ or N	↑	↑	Autosomal recessive; very high serum levels of 1,25(OH) <sub>2</sub> D <sub>3</sub> ; may result from 1,25(OH) <sub>2</sub> D receptor-binding disorder

N = normal

## Table 7-1 • COMMON CAUSES OF ABNORMAL METABOLISM OF CALCIUM AND PHOSPHORUS

The **most common form of nonnutritional rickets is familial, primary hypophosphatemia** (X-linked dominant) in which phosphate reabsorption is defective, and conversion of 25(OH)D to 1,25(OH)<sub>2</sub>D in the proximal tubules of the kidneys is abnormal. This results in low serum 1,25(OH)<sub>2</sub>D, low–normal serum calcium, moderately low serum phosphate, and elevated serum alkaline phosphatase levels. Additionally hyperphosphaturia without evidence of hyperparathyroidism is present. Children at the age of walking present with smooth lower-extremity bowing (as compared to angular bowing of calcium-deficient rickets), a waddling gait, genu varum, genu valgum, coxa vara, and short stature. Other findings of calcium-deficient rickets (myopathy, rachitic rosary, pectus deformities, tetany) usually are not seen. Familial hypophosphatemia can cause intraglobular dentin deformities, whereas calcium-deficient rickets causes enamel defects. Radiologic findings include coarse-appearing trabecular bone and widening, fraying, and cupping of the metaphysis of the proximal and distal tibia, distal femur radius, and ulna.

## COMPREHENSION QUESTIONS

- 7.1 A 14-month-old child has lower-extremity bowing, a waddling gait, and genu varum, and is at the 5th percentile for height. Laboratory data include low–normal serum calcium, moderately low serum phosphate, and elevated serum alkaline phosphatase levels, hyperphosphaturia, and normal parathyroid levels. Which of the following is the most likely diagnosis?
- A. Fanconi syndrome
  - B. Genetic primary hypophosphatemia
  - C. Malabsorption of vitamin D
  - D. Phosphate malabsorption
  - E. Renal osteodystrophy
- 7.2 An 8-month-old African-American baby arrives to the emergency department with his mother with the complaint of decreased left arm movement. He is born after a normal term pregnancy, has had no medical

problems, and was in good health when his mother dropped him off at the day care center. Upper arm radiographs show a left humerus spiral fracture. Which of the following is the most appropriate next step in management?

- A. Admit the child and call child protective services.
- B. Obtain serum 1,25(OH)<sub>2</sub>D levels.
- C. Order serum alkaline phosphatase levels.
- D. Obtain stool for analysis for fat-soluble vitamins.
- E. Send chromosome sample for osteogenesis imperfecta analysis.

7.3 The diet of a 3-year-old child with cystic fibrosis should be supplemented with which of the following?

- A. Folate
- B. Sodium
- C. Vitamin C
- D. Vitamin B<sub>12</sub>
- E. Vitamin D

7.4 A 5-year-old girl is somewhat short and has mild leg bowing. Her medical history is significant only for well-controlled seizure disorder. Serum calcium, phosphorus, and alkaline phosphatase levels and urinary amino acid concentration are normal. A bone age is notable for abnormal distal radius and ulna mineralization. Which of the following is the most likely diagnosis?

- A. Cystic fibrosis
- B. Fanconi syndrome
- C. Genetic primary hypophosphatemia
- D. Rickets associated with anticonvulsive drug use
- E. Schmid metaphyseal dysplasia

## ANSWERS



- 7.1 B. Lower-extremity bowing, low–normal calcium and phosphate levels, and normal parathyroid hormone levels suggest familial primary hypophosphatemia.
- 7.2 A. A spiral fracture of the humerus is suspicious but not diagnostic for child abuse. While further laboratory testing is appropriate, the next step in the management of this child is to provide a safe environment until more data are available.
- 7.3 E. In addition to pancreatic enzyme replacement therapy, supplementation with fat-soluble vitamins (A, D, E, and K), often iron, and sometimes zinc is recommended.
- 7.4 E. All of the rickets syndromes present with elevated alkaline phosphatase levels. Schmid metaphyseal dysplasia, an autosomal dominant condition, presents in a similar way with short stature, leg bowing, and waddling gait. Radiographs show irregular long bone mineralization. Biochemically, Schmid-type metaphyseal dysostosis present with normal serum calcium, phosphorus, and alkaline phosphatase activity and normal urinary amino acid levels.
- 

### CLINICAL PEARLS

- Nutritional rickets (inadequate dietary vitamin D or sunlight exposure) is rare in healthy children in industrialized countries. Medical conditions (liver or renal failure) or abnormalities in calcium and phosphorus metabolism usually are responsible.
  - Primary hypophosphatemia (X-linked dominant) is the most common cause of nonnutritional rickets; proximal kidney tubule defects in phosphate reabsorption and conversion of 25(OH)D to 1,25(OH)<sub>2</sub>D are seen. Findings include low–normal serum calcium, moderately low serum phosphate, elevated serum alkaline phosphatase, and low serum 1,25(OH)<sub>2</sub>D levels, hyperphosphaturia, and no evidence of hyperparathyroidism.
- 

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## CASE 8

A family reports that their 5-year-old son has been increasingly confused over the last several hours. His emergency department vital signs show a heart rate of 180 beats/min, a blood pressure of 80/50 mm Hg, a temperature of 36.1 °C (97°F), and slow, deep respirations. His capillary refill is 5 seconds, and he has skin tenting as well as altered mental status. His mother reports that he has had a several pounds of weight loss over the last few weeks, has been increasingly tired for several days, and that she has been concerned about his 2- or 3-day history of thirst, frequent daytime urination, and new onset of nocturnal enuresis.

- What is the most likely diagnosis?
- What is the best therapy?

## ANSWERS TO CASE 8: **Diabetic Ketoacidosis**

*Summary:* A 5-year-old with weight loss, polydipsia, and polyuria who presents with dehydration and Kussmaul breathing.

- **Most likely diagnosis:** Diabetic ketoacidosis (DKA).
- **Best therapy:** Fluid rehydration, insulin, and close monitoring of serum glucose level and acidemia.

## ANALYSIS

### *Objectives*

1. Understand the presentation of patients in DKA.
2. Appreciate the initial treatment strategies in the management of DKA.
3. Become familiar with pitfalls in the treatment of DKA.

### *Considerations*

This patient is **in extremis**. He is tachycardic, hypotensive, hypothermic, and has delayed capillary refill with tenting of the skin. The **ABCs** of medicine apply. He is confused but not obtunded; he probably requires neither his Airway controlled nor his **B**reathing regulated. His examination suggests at least 10% dehydration; his **C**irculatory status is marginal and requires rapid volume restoration. His history and physical examination suggest diabetes; a finger-stick glucose test confirms the diagnosis. The therapy for DKA rests on: (1) aggressive volume repletion, (2) glucose control with insulin, and (3) correction of metabolic abnormalities.

APPROACH TO:

**Diabetic Ketoacidosis**

## DEFINITIONS

**KETOACIDOSIS:** A condition resulting from deficient insulin availability, leading to lipid oxidation and metabolism rather than glucose metabolism.

The insulin absence results in free fatty acid (FFA) released from adipose tissue and in unregulated hepatic FFA oxidation and ketogenesis.

**TYPE I DIABETES:** Known by a variety of names, it is caused by a severe endogenous insulin deficiency and a requirement for exogenous insulin to prevent ketoacidosis.

**TYPE II DIABETES:** Known by a variety of names, it usually consists of tissue-level insulin resistance (although exogenous insulin is often required) and rarely leads to ketoacidosis.

**KUSSMAUL BREATHING:** Deep, rapid respirations associated with acidosis.

## CLINICAL APPROACH

**Patients with DKA represent a medical emergency.** Such patients may require intubation, but usually this is seen later in the disease course. Children more commonly present signs and symptoms of severe dehydration and acidosis. **The history often is positive for polyuria, polydipsia, nausea, vomiting, and abdominal complaints. Hypothermia, hypotension, Kussmaul respirations, and acetone on the breath are common.** As these signs and symptoms may be nonspecific, especially in younger children, a high index of suspicion is required to make the diagnosis.

Laboratory data demonstrate an **elevated glucose level** (often 400-800 mg/dL), **metabolic acidosis** (with anion gap, ie, excess endogenous anion production such as from lactic acid), and **hyperketonemia**. Serum electrolyte levels usually show hyponatremia and normal or slightly elevated potassium (despite potentially serious intracellular potassium depletion). Elevated blood urea nitrogen and creatinine levels are commonly seen, reflecting the dehydration. White blood cell counts (WBCs) often are elevated, especially if a bacterial infection is exacerbating the condition.

**Treating DKA includes initial vascular volume expansion (often with normal saline) and then correction of the hyperglycemia and hyperketonemia.** Intravenous (IV) fluid boluses sufficient to stabilize the heart rate and blood pressure are often required, and then a slower IV rate (usually a saline solution with or without some glucose) to replace fluid losses and to ensure adequate urine flow is initiated. **Potassium is added to IV fluids after urine output** is established to counteract the patient's total body potassium depletion (treatment of the hyperglycemia and acidosis drives potassium intracellularly; hypokalemia is an avoidable life-threatening complication). A continuous insulin infusion at a rate of approximately 0.1 U/kg/h is also started (a bolus of 0.1 U/kg is often given initially), with the IV rate adjusted based on the results of hourly glucose measurements. Glucose is added to IV fluids when the serum glucose level drops to approximately 250 or 300 mg/dL, and additional insulin rate adjustments are made based on serum glucose levels. **The low plasma pH and elevated serum ketone levels will correct significantly in the first 8 to 10 hours;** the serum bicarbonate level may remain low for 24 hours or more. Improvement is characterized by

a decrease in IV insulin doses and resolution of the ketonuria; then, the patient can take oral feedings, and insulin is converted from the IV to subcutaneous route.

Several pitfalls should be avoided during the treatment of DKA. Intravenous fluids with insulin and **improvement in acidosis levels often are associated with a fall in serum potassium levels**; addition of potassium to the IV fluids usually is indicated to prevent serious hypokalemia. Bicarbonate infusion usually is avoided except in extreme situations, because it may: (1) precipitate hypokalemia, (2) shift the oxygen dissociation curve to the left, worsening organ oxygen delivery, (3) overcorrect the acidosis, and (4) result in worsening cerebral acidosis while the plasma pH is being corrected (transfer into the cerebrum of CO<sub>2</sub> formed when the bicarbonate is infused in an acid serum). Cerebral edema (etiology unknown) sometimes occurs, manifesting as headache, personality changes, vomiting, and decreased reflexes. Treatment of cerebral edema consists of reduction in IV fluid, administration of IV mannitol, and hyperventilation. **Episodes of DKA (especially in the known diabetic) can be precipitated by bacterial infection.** An **evaluation for infection sources** with institution of antibiotics (if appropriate) is required.

## COMPREHENSION QUESTIONS

- 8.1 A 14-year-old adolescent girl from another state was monitored for 7 years for a history of insulin-dependent diabetes mellitus. At your clinic her hemoglobin A1C is 14.9%. This laboratory test indicates which of the following?
- A. Her glucose control is poor.
  - B. She does not have insulin-dependent diabetes.
  - C. She has entered the “honeymoon phase” of her diabetes.
  - D. She has an underlying infection.
  - E. She is demonstrating the Somogyi phenomenon.
- 8.2 Six months after being diagnosed with what appears to be insulin-dependent diabetes, the 5-year-old in the case presentation has a significant decrease in his insulin requirement. Which of the following is the most likely explanation?

- A. His diagnosis of insulin-dependent diabetes was incorrect.
  - B. He had a chronic infection that is now under control.
  - C. He has followed his diabetes diet so well that he requires less insulin.
  - D. He is demonstrating the Somogyi phenomenon.
  - E. He has entered the “honeymoon phase” of his diabetes.
- 8.3 A 15-year-old adolescent girl has experienced abdominal pain, vomiting, and lethargy for 3 days. Her chest and throat examinations are clear, but her abdominal examination is significant for right lower quadrant pain. Rectal examination is equivocal for pain, and her pelvic examination is remarkable for pain upon movement of her cervix. Laboratory data include a white blood cell count of  $18,000/\text{mm}^3$ , serum glucose level of 145 mg/dL, and serum bicarbonate level of 21 mEq/dL. Her urinalysis is remarkable for 1+ white blood cells, 1+ glucose, and 1+ ketones. Which of the following is the most likely diagnosis?
- A. Appendicitis
  - B. Diabetic ketoacidosis (DKA)
  - C. Gastroenteritis
  - D. Pelvic inflammatory disease (PID)
  - E. Right lower lobe pneumonia
- 8.4 A 16-year-old adolescent girl has enuresis, frequent urination, a white vaginal discharge, and a dark rash around her neck. She is greater than the 95th percentile for her age. Her serum glucose level is 250 mg/dL, and her urinalysis is positive for 2+ glucose but is otherwise negative. Which of the following is the most likely diagnosis?
- A. Chemical vaginitis
  - B. Chlamydia cervicitis
  - C. Psoriasis
  - D. Type II diabetes
  - E. Urinary tract infection (UTI)

## ANSWERS



- 8.1 A. The patient most likely has poor diabetes control. The hemoglobin A1C test, commonly used to follow glucose control, reflects the average glucose levels over the previous 2 or 3 months. The hemoglobin A1C goal for most diabetics is 6% to 9%. Levels greater than 12% suggest poor control, and levels of 9% to 12% represent fair control. In the Somogyi phenomenon, a patient has nocturnal hypoglycemic episodes manifested as night terrors, headaches, or early morning sweating and then presents a few hours later with hyperglycemia, ketonuria, and glucosuria. Counter-regulatory hormones, in response to the hypoglycemia, cause the hyperglycemia.
- 8.2 E. Up to 75% of newly diagnosed diabetics have a progressive decrease in the daily insulin requirement in the months after their diabetes diagnosis; a few patients temporarily require no insulin. This “honeymoon” period usually lasts a few months, and then an insulin requirement returns. Patients are told that the “honeymoon” period is not a cure and that they should expect a return to insulin requirement.
- 8.3 D. The patient likely has PID; glucosuria is a stress response to the infection and does not represent glucose metabolism problems. All of the options in the question can cause abdominal pain. Although diabetes mellitus is in the differential, DKA more likely presents with ketoacidosis (significantly decreased serum bicarbonate levels) and high serum glucose levels.
- 8.4 D. The description is of an obese adolescent female with candida vaginitis (the vaginal discharge) and acanthosis nigricans (the nuchal dark rash) consistent with type II diabetes. This condition is far more common in overweight children, especially those with a family history of the condition.
- 

## CLINICAL PEARLS

- Diabetic ketoacidosis (DKA) is a medical emergency that can present with nonspecific signs of dehydration, polyuria, nausea, vomiting, and abdominal complaints. Hypothermia, hypotension, Kussmaul respirations, and acetone on the breath are also seen. A high index of suspicion is required to make the diagnosis, especially in the younger child.

- Cerebral edema is a potentially life-threatening complication in diabetic ketoacidosis treatment presenting as headache, personality changes, vomiting, and decreased reflexes.
  - Electrolyte disturbances are common in diabetic ketoacidosis. Hypokalemia can occur during treatment if adequate sources are not provided. Bicarbonate administration usually is avoided except in extreme situations for a variety of physiologic reasons.
- 

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## CASE 9

An 8-year-old child presents to the emergency department with the complaint of right-sided weakness. The child is one of your well-known sickle cell disease (SCD) patients having been followed by your practice since birth. The child's previous history has been relatively benign with only two

previous hospitalizations, once at 6 months for fever and another at 12 months for a swollen, painful left wrist.

- ▶ What is the next step in the care of this patient?
- ▶ What long-term strategies might be employed to prevent recurrence?

### ANSWER TO CASE 9: **Sickle Cell Disease with Probable Stroke**

*Summary:* A healthy 8-year-old-child known to have SCD presents with acute onset of weakness.

- **Next step:** Admit to the hospital (probably the intensive care unit) and arrange for a simple or partial exchange transfusion to reduce the amount of circulating sickle cells and thus reduce the chances for further neurologic damage.
- **Long-term strategy:** This child's chance of a second stroke in the upcoming 2 years is approximately 70% to 80%. Thus, chronic transfusion therapy is indicated to reduce the risk of such neurologic events.

## ANALYSIS

### *Objectives*

1. Become familiar with the goals of the routine well-child (or health supervision) session for a patient with SCD.
2. Learn the common complications and treatment strategies for a child with SCD.

### *Considerations*

Well-child care for healthy children typically is uncomplicated. For children with special needs, such as SCD or Down syndrome, guidelines outline their specific considerations. For children with multiple handicaps, such as those resulting from extreme prematurity, no specific guidelines exist; the providers adapt national "well-child care" guidelines as appropriate.

APPROACH TO:

## **Sickle Cell Disease**

### **CLINICAL APPROACH**

Goals of a health supervision visit for all children including those with sickle cell and other disease incorporate evaluating a child's physical, developmental, psychosocial, and educational status to identify problems early; prompt intervention then can be instituted. Anticipatory guidance aims to foster good health habits, prevent illness, and assist in family communication. For the child with a diagnosis such as SCD, additional strategies are also employed including ensuring the child is linked to a comprehensive SCD program.

Hemoglobinopathies such as SCD are often diagnosed at birth as part of each state's newborn screening program. Routine care for the child with SCD then can be implemented, which typically includes such things as initiation of daily penicillin therapy by 2 months of age and folate by 6 months of age. Special vaccinations for these children include administration at 2 years of age—meningococcal and the 23-valent polysaccharide pneumococcal vaccines; additional doses of these vaccines may be required. Additional laboratory, radiologic, and other testing also may be indicated.

### **ILLNESSES IN AN SCD PATIENT REQUIRING URGENT MEDICAL CARE**

Children with SCD are at high risk for sepsis; those who present with temperatures greater than approximately 38.5°C require evaluation and initiation of antibiotic therapy. Hospital admission is indicated for febrile young children, all children who have evidence of toxicity, or children whose laboratory evaluation is of concern.

Pain crises are not uncommon among children with SCD. Children whose pain is inadequately controlled with home medications regimens must be evaluated. Additional pain medications, such as morphine or hydromorphone, along with hydration may be attempted in the outpatient setting. If more than one or two doses of these additional pain medications are required, inpatient hospitalization is required.

Children with SCD who have significant respiratory symptoms such as severe cough, shortness of breath, or chest pain may be exhibiting symptoms of acute chest syndrome. Should these children with lower respiratory symptoms have hypoxemia and a new infiltrate on chest radiograph, hospital admission is warranted. Therapies might include oxygen, hydration, blood transfusion, pain control, and antibiotics. Close observation of respiratory failure is warranted.

Parents of the child with SCD are taught to palpate the abdomen of their younger children to observe for splenic enlargement. A child who has abdominal pain, distension, or acute enlargement of the spleen likely has acute splenic sequestration and requires hospitalization, possibly in the intensive care unit, to observe for cardiovascular collapse. Blood transfusions, perhaps even emergently, may be required and will be life-saving. As the child ages the spleen usually auto-infarcts, eliminating the SCD complication of splenic sequestration but increasing the odds of an encapsulated organism infection.

About 10% of children with SCD have acute stroke. Symptoms might include paresis, aphasia, seizures, cranial nerve palsy, headache, or coma; all such children are admitted to the hospital. Emergency neuroimaging is warranted, repeated neurologic examinations are conducted, and partial or simple transfusions are performed to reduce the percentage of sickle cells. Physical therapy and rehabilitation are provided as the patient recovers. Chronic transfusions are instituted to reduce the risk of recurrence. As part of the routine well-child care of an SCD patient, transcranial Doppler (TCD) ultrasonography is often recommended to identify those with increased flow velocity in the large cerebral blood vessels and thus at high-risk for developing a first stroke. Chronic transfusion among these high-risk children has resulted in reduced risk of first stroke.

A child with SCD who presents with a significant increase in pallor, fatigue, or lethargy may be exhibiting signs of aplastic crisis. These children will have a hemoglobin level below their normal baseline and a low reticulocyte count. These children require hospitalization to observe for evidence of cardiovascular collapse. Blood transfusions may be required.

A boy with SCD who has a priapism episode persisting for more than 3 to 4 hours must be evaluated by a urologist. Intravenous fluid hydration and pain control are provided; ice is not to be used. The urologist may be required to aspirate and irrigate the corpora cavernosa to achieve detumescence. Failure of 3 or 4 aspirations in the outpatient setting requires more extensive inpatient

management including exchange blood transfusions, further pain control, and additional surgical interventions.

Significant vomiting or diarrhea in the patient with SCD puts the patient at risk for dehydration and a vaso-occlusive crisis. Intravenous fluids until the patient is able to tolerate liquids orally may be required.

## COMPREHENSION QUESTIONS

- 9.1 A 14-year-old girl is known to have SCD. Over the previous 2 or 3 months, she has been having increasingly frequent episodes of right upper quadrant, cramping pain. Which of the following strategies is likely to identify her medical condition?
- A. Measure hepatitis B surface antigen and antibody levels.
  - B. Obtain urine for routine analysis and culture.
  - C. Obtain an ultrasound of her gallbladder.
  - D. Order a chest radiograph for new infiltrates.
  - E. Measure via echocardiogram her cardiac output.
- 9.2 Appropriate advice for a mother of a 2-week-old child identified on newborn state screening to have SCD includes which of the following?
- A. Initiation of iron therapy.
  - B. Emergent genetic testing of both parents for hemoglobinopathy status.
  - C. Initiation of hydroxyurea therapy.
  - D. Purchase of an apnea monitor.
  - E. Enrollment in a comprehensive sickle cell program.
- 9.3 During the triage of a “well-child” visit, the staff record that the parents of a previously healthy 5-month-old offer a great amount of information. Which of the following bits of information is of most concern?
- A. A diet that includes baby cereal, five different baby vegetables, and one baby fruit.
  - B. Consuming 32 oz of infant formula per day.
  - C. Intermittent tugging on the ears.
  - D. The child appears to be more pale than usual.

E. Rolling from front to back but not back to front.

9.4 Which of the following statements about “routine” procedures for an SCD patient is accurate?

A. All SCD children have baseline and then periodic CBC and reticulocyte measurement screenings beginning at about 2 months.

B. To reduce the risk of sepsis, polysaccharide pneumococcal 23 vaccines are administered at 2, 4, and 6 months of age.

C. To identify new infiltrates, chest radiographs are obtained at all routine visits beginning at about 12 months of age.

D. Yearly gallbladder ultrasounds are indicated beginning at adolescence to identify the presence of stones.

E. Human papilloma virus vaccines are contraindicated in the SCD population.

## ANSWERS

9.1 C. The child presented has pain referred to the right upper quadrant; she is at high risk for developing gallstones because of her SCD. The one test likely to identify the stones is the ultrasound. Part of her routine childhood immunizations should have been vaccination for hepatitis B, thus making this type of hepatitis unlikely. She may need periodic chest radiographs or echocardiograms, especially if she has evidence of acute chest syndrome or chronic cardiac/pulmonary disease, but the case as presented does not suggest such findings.

9.2 E. This child must be enrolled in a comprehensive SCD program to ensure the best possible outcome. At 2 weeks of age, the child has no reason to be iron deficient, and combined with future blood transfusions that may be required, iron therapy could result in iron overload. The newborn state screen has shown the child to have SCD and that both parents have at least a single sickle cell gene; further testing of the family may be warranted but not as an emergency. Hydroxyurea is used to increase the levels of fetal hemoglobin; this child already has significant quantities of that hemoglobin. SCD is not an indication for an apnea monitor.

- 9.3 D. All of the items presented are normal for the child's age except increasing pallor, which may be due to splenic sequestration of aplastic anemia.
- 9.4 A. SCD patients require baseline and periodic blood counts as described. The 23 valent polysaccharide pneumococcal vaccine is initiated at 2 years of age, while the conjugate pneumococcal vaccine is administered at the younger ages outlined. Chest radiographs typically are obtained at approximately 2 years of age and periodically thereafter for screening purposes, for recent acute chest syndrome, or if the child has chronic cardiac or pulmonary disease. Ultrasounds of the gallbladder are reserved for patients with symptoms referable to that area.
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### CLINICAL PEARLS

- Children with SCD who have fever (risk of sepsis), pallor (aplastic crisis), abdominal pain or distension (splenic sequestration), pain crisis, evidence of lower respiratory disease (acute chest syndrome), priapism, new neurologic findings (stroke), or dehydration must be evaluated urgently.
  - Additions to routine care required for all children include initiation of penicillin and folate therapies as well as initiation of meningococcal and polysaccharide vaccines at early-than-typical ages.
  - A variety of screening tests, such as routine CBC and reticulocyte measurements, begin at 2 months of age or at diagnosis.
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## CASE 10

A 4-year-old boy has a 2-day history of runny nose, productive cough, and wheezing. Subjective fever and decreased appetite also were noted today. He has no known cardiorespiratory disease, and his immunizations are current. His two younger siblings are recovering from “chest colds.” On examination, he is febrile to 103.2°F (39.6°C), with a respiratory rate of 22 breaths/min. His examination is remarkable for congested nares, clear rhinorrhea, coarse breaths sounds in all lung fields, and bibasilar end-expiratory wheezes.

- What is the most likely diagnosis?
- What is the next step in evaluation?

## ANSWERS TO CASE 10: **Pneumonia**

*Summary:* A toddler presents with cough, fever, and an abnormal chest examination.

- **Most likely diagnosis:** Pneumonia.
- **Next step in evaluation:** A chest x-ray (CXR) often is indicated to ascertain if radiographic changes support clinical findings. In addition to chest radiography, pulse oximetry and selected laboratory tests (complete blood count [CBC], blood culture, and nasal wash for selected viral antigens) may help elucidate the etiology and extent of infection, as well as direct possible antimicrobial therapy.

## ANALYSIS

### *Objectives*

1. Describe the etiologies of pneumonia and their age predilections.
2. Describe various clinical and radiographic findings in pneumonia.
3. Describe the evaluation and treatment of pneumonia.

### *Considerations*

The most important initial goal in managing this patient is to ensure adequacy of the **ABCs** (maintaining the **A**irway, controlling the **B**reathing, and ensuring adequate **C**irculation). A patient with pneumonia may present with varying degrees of respiratory compromise. Oxygen may be required, and in severe cases respiratory failure may be imminent, necessitating intubation and mechanical ventilation. The patient with pneumonia and sepsis also may have evidence of circulatory failure (septic shock) and require vigorous fluid resuscitation. After the basics of resuscitation have been achieved, further evaluation and management can be initiated.

APPROACH TO:

**The Child with Pneumonia**

## DEFINITIONS

**RALES:** Wet or “crackly” inspiratory breath sounds due to alveolar fluid or debris; usually heard in pneumonia or congestive heart failure (CHF).

**PLEURAL RUB:** Inspiratory and expiratory “rubbing” or scratching breath sounds heard when inflamed visceral and parietal pleurae come together.

**STACCATO COUGH:** Coughing spells with quiet intervals, often heard in pertussis and chlamydial pneumonia.

**PLEURAL EFFUSION:** Fluid accumulation in the pleural space; may be associated with chest pain or dyspnea; can be transudate or exudate depending on results of fluid analysis for protein and lactate dehydrogenase; origins include cardiovascular (congestive heart failure), infectious (mycobacterial pneumonia), and malignant (lymphoma).

**EMPHYEMA:** Purulent infection in the pleural space; may be associated with chest pain, dyspnea, or fever; usually seen in conjunction with bacterial pneumonia or pulmonary abscess.

**PULSE OXIMETRY:** Noninvasive estimation of arterial oxyhemoglobin concentration (SPO<sub>2</sub>) using select wavelengths of light.

## CLINICAL APPROACH

Pneumonia or lower respiratory tract infection (LRTI) is a diagnosis made clinically and radiographically. The typical pediatric patient with pneumonia may have traditional findings (fever, cough, tachypnea, and toxicity) or very few signs, depending on the organism involved and the patient's age and health status.

### *Pathophysiology*

Lower respiratory tract infection (LRTI) typically begins with organism acquisition via inhalation of infected droplets or contact with a contaminated surface. Depending on the organism, spread to distal airways occurs over varying intervals. Bacterial infection typically progresses rapidly over a few days; viral pneumonia may develop more gradually. With infection progression, an inflammatory cascade ensues with airways affected by humoral and cellular mediators. The resulting milieu adversely affects ventilation–perfusion, and respiratory symptoms develop.

### *Clinical and Radiologic Findings*

The pneumonia process may produce few findings or may present with increased work of breathing manifested as nasal flaring, accessory muscle use, or tachypnea, the latter being a relatively sensitive indicator of pneumonia. Associated symptoms may include malaise, headache, abdominal

pain, nausea, or emesis. Toxicity can develop, especially in bacterial pneumonia. Fever is not a constant finding. Subtle temperature instability may be noted in neonatal pneumonia. Clinically, pneumonia can be associated with decreased or abnormal breathing (rales or wheezing). Chest examination may be equivocal, especially in the neonate. Hypoxia can be seen. Pneumonia complications (pleural effusion) may be identified by finding localized decreased breath sounds or rubs.

Radiographic findings in LRTI may be limited, nonexistent, or lag the clinical symptoms, especially in the dehydrated patient. Findings may include single or multilobar consolidation (pneumococcal or staphylococcal pneumonia), air trapping with a flattened diaphragm (viral pneumonia with bronchospasm), or perihilar lymphadenopathy (mycobacterial pneumonia). Alternatively, an interstitial pattern may predominate (mycoplasmal pneumonia). Finally, pleural effusion and abscess formation are more consistent with bacterial infection.

### ***Causative Organisms***

LRTI occurs more frequently in the fall and winter and with greater frequency in younger patients, especially those in group environments (large households, day care facilities, and elementary schools). When all age groups are considered, approximately 60% of pediatric pneumonias are bacterial in origin, with pneumococcus topping the list. Viruses (respiratory syncytial virus [RSV], adenovirus, influenza, parainfluenza, enteric cytopathic human orphan [ECHO] virus, and coxsackie virus) run a close second.

Identifying an organism in pediatric pneumonia may prove difficult; causative organisms are identified in only 40% to 80% of cases. Routine culturing of the nasopharynx (poor sensitivity/specificity) or sputum (difficulty obtaining specimens in young patients) usually is not performed. Thus, diagnosis and treatment usually are directed by a patient's symptoms, physical and radiographic findings, and age.

**In the first few days of life, *Enterobacteriaceae* and group B *Streptococcus* (GBS) are the primary bacterial etiologies; other possibilities include *Staphylococcus aureus*, *Streptococcus pneumoniae* (pneumococcus), and *Listeria monocytogenes*.** In the newborn with pneumonia, broad-spectrum antimicrobials (ampicillin with either gentamicin or cefotaxime) are customarily prescribed. **During the first few months of**

life, *Chlamydia trachomatis* is a possibility, particularly in the infant with staccato cough and tachypnea, with or without conjunctivitis or known maternal chlamydia history. These infants also may have eosinophilia, and bilateral infiltrates with hyperinflation on chest radiograph; treatment is erythromycin. Viral etiologies include herpes simplex virus (HSV), enterovirus, influenza, and RSV; of these, HSV is the most concerning and prevalent viral pneumonia in the first few days of life. Intravenous acyclovir is an important consideration if HSV is suspected.

Beyond the newborn period and through approximately 5 years of age, viral pneumonia is common; adenovirus, rhinovirus, RSV, influenza, and parainfluenza are possibilities. Bacterial etiologies include pneumococcus and nontypeable *Haemophilus influenzae*. Patients with nasal and chest congestion with increased work of breathing, wheezing, and hypoxemia regularly present to the emergency room during the winter months and are admitted for observation, oxygen, and bronchodilator therapies. The diagnosis of a viral process may be made clinically or with CXR findings (perihilar interstitial infiltrates). Nucleic acid polymerase chain reaction (PCR) amplification of secretions from a nasal swab or wash often is performed to confirm a viral etiology. A mixed viral and bacterial pneumonia can be present in approximately 20% of patients. Antibacterial coverage should be considered if the clinical scenario, examination, or x-ray findings suggest bacterial infection.

The pediatric patient older than approximately 5 years of age with LRTI typically has *Mycoplasma*. However, most of the viral and bacterial etiologies previously listed are possible, except GBS and *Listeria*.

Antibiotics in this age group are directed toward *Mycoplasma* and typical bacteria (pneumococcus). Treatment options include macrolides (azithromycin) or cephalosporins (ceftriaxone or cefuroxime).

Pneumonia in the intubated intensive care patient with central lines may be related to *Pseudomonas aeruginosa* or fungal species (*Candida*). *Pseudomonas* and *Aspergillus* are possibilities in the patient with chronic lung disease (cystic fibrosis). Varicella-zoster virus should be considered in the patient with typical skin findings and pneumonia; cytomegalovirus (CMV) if concomitant retinitis is present; *Legionella pneumophila* if the patient has been exposed to stagnant water; and *Aspergillus* if a patient has refractory asthma or a classic “fungal ball” on chest radiograph. Travel to the

southwestern United States may expose patients to *Coccidioides immitis*, infected sheep or cattle to *Coxiella burnetii*, and spelunking or working on a farm east of the Rocky Mountains to *Histoplasma capsulatum*.

**One important subset of LRTI is tuberculosis (TB).** *Mycobacterium tuberculosis* has become more problematic over the past decade; multidrug resistance is increasingly seen. Patients may present with symptoms ranging from a traditional cough, bloody sputum, fever, and weight loss to subtle or nonspecific symptoms. A positive purified protein derivative (PPD) is defined by induration diameter in the context of a patient's exposure history, radiographic findings, and immune status. For instance, 5-mm induration may be considered a "positive PPD" at 48 to 72 hours in a patient with confirmed exposure, abnormal chest radiograph, or immunodeficiency. This same measurement in an otherwise healthy child without exposures would not be considered positive. Possible sources for acid-fast bacilli for stain and culture (depending on the age of the patient) include sputum samples, first-morning gastric aspirates, cerebrospinal fluid, bronchial washes or biopsy obtained through bronchoscopy, and empyema fluid analysis or pleural biopsy if surgical intervention is required. Standard antituberculous therapy, while awaiting culture and sensitivities, includes isoniazid, rifampin, and pyrazinamide. For possible drug-resistant organisms, ethambutol can be added temporarily as long as visual acuity can be followed. The typical antibiotic course consists of an initial phase of approximately 2 months' duration on three or four medications, followed by a continuation phase of 4 to 10 months on isoniazid and rifampin. Therapy for 9 to 12 months is recommended for CNS or disseminated TB. Ultimately, total therapy duration is dependent upon the extent of imaging abnormalities, resistance patterns, and results of follow-up sputum samples in the age-appropriate patient. Directly observed therapy should be routinely advised.

## COMPREHENSION QUESTIONS

- 10.1 A 6-week-old boy, born by vaginal delivery after an uncomplicated term gestation, has experienced cough and "fast breathing" for 2 days. His mother relates that he has a 1-week history of nasal congestion and watery eye discharge, but no fever or change in appetite. He has a temperature of 99.4°F (37.4°C) and a respiratory rate of 44 breaths/min. He has nasal congestion, clear rhinorrhea, erythematous conjunctivae

bilaterally, and watery, right eye discharge. His lungs demonstrate scattered crackles without wheezes. Which of the following is the most likely pathogen?

- A. *C trachomatis*
- B. *L monocytogenes*
- C. Respiratory syncytial virus
- D. Rhinovirus
- E. *S pneumoniae*

10.2 A 2-year-old girl has increased work of breathing. Her father notes she has had cough and subjective fever over the past 3 days. She has been complaining that her “belly hurts” and has experienced one episode of posttussive emesis, but no diarrhea. Her immunizations are current, and she is otherwise healthy. Her temperature is 102°F (38.9°C). She is somnolent but easily aroused. Respirations are 28 breaths/min, and her examination is remarkable for decreased breath sounds at the left base posteriorly with prominent crackles. Which of the following acute interventions is the next best step in your evaluation?

- A. Blood culture
- B. Chest radiography
- C. Pulse oximetry
- D. Sputum culture
- E. Viral nasal swab

10.3 You are evaluating a previously healthy 8-year-old boy with subjective fever, sore throat, and cough over the past week. There has been no rhinorrhea, emesis, or diarrhea, and his appetite is unchanged. According to your clinic records, his immunizations are current and his weight was at the 25th percentile on his examination 6 months ago. Today, he is noted at the 10th percentile for weight. He is afebrile, with clear nares and posterior oropharynx, and a normal respiratory effort. He has bilateral cervical and right supraclavicular lymphadenopathy. Chest auscultation is notable for diminished breath sounds at the left base. Beyond obtaining a chest radiograph, which of the following is the best next step in your evaluation?

- A. Rapid strep throat swab
- B. Viral nasal swab
- C. PPD placement
- D. Lymph node biopsy
- E. *Bordetella pertussis* direct fluorescent antibody testing

10.4 A 13-year-old adolescent female complains of dry cough, slight fever, and fatigue over the past 2 weeks. She noted increased chest congestion and coughing yesterday when walking outside in the cold air. She denies nasal congestion, rhinorrhea, emesis, or diarrhea. Her mother declares her daughter is generally healthy with a history of only summertime allergies. Her vital signs, respiratory effort, and chest examination are normal. Which of the following is the most likely pathogen?

- A. *H influenzae*
- B. *M pneumoniae*
- C. Respiratory syncytial virus
- D. *S aureus*
- E. *S pneumoniae*

## ANSWERS

- 10.1 A. Cough and increased respiratory effort in an afebrile infant with eye discharge are consistent with *Chlamydia*. Transmission typically occurs during vaginal delivery. Approximately 25% of infants born to mothers with *Chlamydia* develop conjunctivitis; about half of these develop pneumonia. Most infants present with respiratory infection in the second month of life, but symptoms can be seen as early as the second week. Inner eyelid swabs are sent for PCR, and oral erythromycin or sulfisoxazole (latter only in infants older than 2 months of age) is given for 2 weeks for either conjunctivitis or pneumonia.
- 10.2 C. Tachypnea and lethargy are prominent in this patient with clinical pneumonia. Pulse oximetry should urgently be performed to ascertain whether oxygen is required. Sputum culturing is reasonable for an older patient who can produce sputum, but an adequate and diagnostically



useful specimen can only be obtained from a 2-year-old by endotracheal aspirate or bronchoscopy. In this otherwise healthy toddler for whom concerns for atypical pneumonia are high, invasive maneuvers are not indicated. Viruses (RSV and adenovirus) are prominent at this age; one might consider performing a nasal swab for viral antigens. Abdominal pain, as noted in this question, can be seen as a presenting symptom in pneumonia, probably as a result of irritation of the diaphragm by pulmonary infection.

- 10.3 C. The scenario is typical for pediatric tuberculosis. Neck and perihilar or mediastinal lymphadenopathy and pulmonary or extrapulmonary manifestations can occur, with miliary disease and meningitis more common in infants and younger children. Fever, weight loss, and lower respiratory tract signs and symptoms (possible left pleural effusion in this patient) are archetypal TB findings. A purified protein derivative (PPD) (usually with control) should be placed, and consideration given to hospitalizing this patient in negative pressure isolation for further evaluation beyond PPD placement (pleurocentesis, bronchoalveolar lavage, gastric aspirates) and possible antituberculous treatment.
- 10.4 B. All of these findings are consistent with mycoplasmal infection (“walking pneumonia”). The incubation period for *Mycoplasma* is 5 to 7 days, and most symptoms are noted during the second to third week of infection. Hemolysis occurs as antibodies attach to red blood cells, prompting reticulocyte production. If necessary, nasopharyngeal aspirate for PCR or measurement of cold agglutinins may help aid in the diagnosis. Auscultatory and radiographic findings vary in this infection; a normal CXR or one with an interstitial pattern, effusion, or atelectasis could be seen.

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## CLINICAL PEARLS

- The etiology of pneumonia varies according to the patient’s age. Neonates have the greatest risk of group B *Streptococcus*, toddlers are more likely to have respiratory syncytial virus, and adolescents usually contract *Mycoplasma*.
- Efforts in tuberculosis management should be directed toward isolating an organism and obtaining sensitivities, thus allowing selection of the optimal antituberculous regimen.

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### CASE 11

You are moonlighting in a rural emergency room when a father rushes his 3-year-old daughter into the waiting area. You quickly determine that the child had been playing with her chihuahua at a relative's farm where they were spraying for insects in a field. While at the farm she developed abdominal cramping, cough, drooling, and tearing. While in route the child seems to be having increased respiratory difficulty, and the dad notes she soiled and urinated upon herself.

- What is the most likely diagnosis?
- How is the diagnosis made?
- What is the best therapy?

## ANSWERS TO CASE 11: **Organophosphate Poisoning**

*Summary:* A 3-year-old, previously healthy child who, while playing where spraying for insects was ongoing, develops salivation, lacrimation, respiratory distress, and gastrointestinal (GI) symptoms.

- **Most likely diagnosis:** Organophosphate poisoning.
- **Making the diagnosis:** High index of suspicion so therapy is not delayed; confirmation via decreased serum pseudocholinesterase and erythrocyte cholinesterase levels.
- **Best therapy:** Decontamination of the child, supportive care, administration of atropine or pralidoxime.

## ANALYSIS

### *Objectives*

1. Understand the signs, symptoms, and treatment of organophosphate poisoning.
2. Be familiar with the treatment options of various commonly ingested agents.

### *Considerations*

This child is demonstrating evidence of organophosphate poisoning, the leading cause of nonpharmaceutical ingestion fatality in children. She was exposed during the spraying for insects in a field, and is at risk for ongoing absorption of toxin until decontamination of her clothing is achieved.

*Note:* For some children exposed to a toxic substance, parents are able to provide a container of the toxic agent. For others either the container is not available or the symptoms are not obviously related to a toxic exposure. In all cases a thorough history and physical examination, along with a high index of suspicion in younger children, is required to ensure the diagnosis of accidental toxic exposure.

### APPROACH TO:

### **Organophosphate Poisoning**

# DEFINITIONS

**NICOTINIC SYMPTOMS:** Cardiac (hypertension, tachycardia, arrhythmia); muscle (fasciculations, weakness, tremors); respiratory failure due to diaphragm paralysis; hypertension.

**MUSCARINIC SYMPTOMS:** Gastrointestinal (emesis, urinary and fecal incontinence); respiratory (bronchorrhea, bronchospasm); cardiac (hypotension, bradycardia); tearing and drooling; miosis.

# CLINICAL APPROACH

Millions of children are poisoned each year with about 90% of exposures occurring in the home. About half of all accidental poisonings occur in children younger than 5 years of age. Children aged from about 6 to 12 years are much less likely to be exposed, and those with toxic exposures beyond 12 years of age often do so intentionally. Death due to accidental poisonings has become unusual since a variety of measures have been implemented, including poison prevention as part of all well-child visits, development of regional poison control centers, child-resistant packaging, and improved medical management.

Organophosphate poisoning can occur across skin or mucous membranes, by inhalation, or by ingestion. Commonly found in such pesticides as parathion, malathion, and diazinon, organophosphates bind irreversibly to cholinesterase of neurons and erythrocytes, as well as to liver pseudocholinesterase. The common finding is failure to terminate the effects of acetylcholine at the receptor sites.

Signs and symptoms of cholinergic excess are often remembered with the mnemonic “dumb bells,” which includes:

D	diarrhea/defecation
U	urination
M	miosis
B	brachycardia
B	bronchorrhea
E	emesis/excitation of muscles
L	lacrimation
S	salivation

In addition to these muscarinic and nicotinic effects, central effects including obtundation, seizures, and apnea are also seen.

Confirmation of the exposure can be confirmed by finding decreased serum pseudocholinesterase and erythrocyte cholinesterase levels, but the correlation of these levels to the magnitude of exposure or the symptoms observed is poor. Thus, a high index of suspicion must be maintained to quickly and accurately diagnose organo-phosphate exposure.

Treatment of the patient exposed to organophosphate consists of rapid decontamination by removing all clothing and washing of all skin surfaces. For ingestions, gastric lavage or activated charcoal may be attempted, but the organophosphate compounds are rapidly absorbed and the benefits somewhat limited. The **ABCs** of medicine apply: preserve the **Airway** (intubation may be required); maintain **Breathing** (excessive secretions may require frequent suctioning); and ensure appropriate **Circulation**.

Two specific therapies to counter the effects of organophosphate poisonings include atropine and pralidoxime. Atropine works by antagonizing the muscarinic receptor; large, repeated, and sometimes continuous doses may be required. Often the amount and number of atropine doses required correlates to the degree of exposure, and may assist in the prediction of course duration. Pralidoxime is a cholinesterase-reactivating oxime, often used for patients with significant muscle weakness, especially if mechanical ventilation is required owing to muscle failure.

Careful attention to a child's environment can help prevent countless instances of toxic ingestion. Counseling parents to "poison proof" their home is a first step toward prevention. Written and video materials are readily available through the American Academy of Pediatrics, local and state health departments, and poison control centers. All families are taught to become familiar with the national network of poison control centers, reached toll-free at 1-800-222-1222.

## COMPREHENSION QUESTIONS

11.1 Students attending a school built in 1951 are at risk for which of the following?

- A. Arsenic
- B. Asbestos

- C. Dichlorodiphenyltrichloroethane (DDT)
  - D. Mercury
  - E. Polychlorinated biphenyls (PCBs)
- 11.2 An 8-year-old, mentally delayed child ingests the contents of a mercury thermometer. Which of the following symptoms are most likely to be seen?
- A. Ataxia, dysarthria, and paresthesias
  - B. Chest pain and dyspnea
  - C. Gingivostomatitis, tremor, and neuropsychiatric disturbances
  - D. No symptoms
  - E. Pulmonary fibrosis
- 11.3 A 4-year-old child is found with a bottle of insecticide that contains arsenic. Which of the following symptoms is most likely to occur?
- A. Bradycardia with third-degree heart block
  - B. Constipation
  - C. Hemorrhagic gastroenteritis with third spacing of fluids
  - D. Hyperreflexia
  - E. Hypothermia
- 11.4 Exposure to environmental toxins can occur in a number of ways. Which of the following is the most likely mechanism of exposure?
- A. Asbestos exposure from hazardous arts and crafts materials
  - B. Exposure of a child to beryllium from the child's parents' clothing
  - C. Iron intoxication from vehicular emissions
  - D. Lead toxicity from ingesting pieces of a pencil
  - E. Transplacental exposure to benzene

## ANSWERS

- 11.1 **B.** Between 1947 and 1973 asbestos was commonly sprayed on school ceilings as a fire retardant. Deterioration results in release of

microscopic fibers into the air. Drop ceilings or placement of barriers usually is sufficient protection against this carcinogen.

- 11.2 D.** The child in the question is unlikely to develop symptoms (the quantity of mercury is small); a larger acute elemental ingestion might result in a variety of gastrointestinal (GI) complaints. If the elemental mercury were in vapor form, GI complaints would be seen, along with fever, chills, headaches, visual changes, cough, chest pain, and possibly pneumonitis and pulmonary edema. Exposure to inorganic mercury salts (pesticides, disinfectants, explosives, dry batteries) can cause gastroesophageal burns, nausea, vomiting, abdominal pain, hematemesis, hematochezia, cardiovascular collapse, or death. Ataxia, dysarthria, and paresthesias are seen in methyl mercury intoxication (contaminated fish exposure). Gingivostomatitis, tremor, and neuropsychiatric disturbances are seen with chronic inorganic mercury intoxication; indeed, the term “mad as a hatter” originates from the occupational hazard of workers’ exposure in the early industrial period to mercury-containing vapors during the process of felt hat making.
- 11.3 C.** Acute arsenic ingestions can cause nausea, vomiting, abdominal pain, and diarrhea. The third spacing and hemorrhage in the gut can lead to hypovolemic shock. Cardiac symptoms include ventricular tachycardia (QT prolongation) and congestive heart failure (CHF). These patients can develop seizures, cerebral edema, encephalopathy, and coma. Early on, patients develop loss of deep tendon reflexes, paralysis, painful dysesthesias, and respiratory failure similar to Guillain-Barré syndrome. Fever, anemia, alopecia, hepatitis, and renal failure also can be seen.
- 11.4 B.** Fat-soluble compounds can be transmitted transplacentally (but benzene would be unusual). Parents’ work clothes can transmit potentially hazardous compounds. Arts and crafts supplies likely do not contain asbestos. Vehicular emissions are responsible for a number of pollutants including lead prior to lead-free gasoline, many of which are carcinogens, but iron intoxication would be unusual. Pencil “lead” is actually graphite (carbon) and not elemental lead.

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## CLINICAL PEARLS

- ▶ Organophosphate poisoning is the leading cause of nonpharmacologic ingestion fatality in the United States.
  - ▶ The mnemonic “dumb bells” outlines the signs and symptoms of cholinergic excess.
  - ▶ Therapy for organophosphate toxicity includes supportive care and use of either atropine or pralidoxime.
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## CASE 12

A mother brings her 2-year-old son to your clinic because she has seen over the last 2 days drops of bright red blood in his diaper with each stool and with wiping. He is eating his regular diet of grilled cheese sandwiches with 20 ounces of milk each day. He has been afebrile with no vomiting or diarrhea. Mom has noted he cries with stooling. Your examination of abdomen is normal. On inspection of the rectal area you find a 7-mm linear split in the posterior midline traversing from the anocutaneous junction to the dentate line. There is also a small skin appendage in the same area. His parents are the only caregivers.

- ▶ What is the most likely diagnosis?



- ▶ What is the best management for this condition?
- ▶ What is your next step in the evaluation?

## ANSWERS TO CASE 12: **Rectal Bleeding**

*Summary:* A 2-year-old boy presents with rectal bleeding and pain on defecation.

- **Most likely diagnosis:** Anal fissure
- **Best management:** Confirm that the red substance is blood by performing a fecal occult blood test. Red-pigmented foods such as gelatin, breakfast cereals, or beets can mimic blood. When the reagent of the fecal occult blood test combines with hemoglobin, a blue color appears. This test is very sensitive. The concomitant rectal exam can assess for impacted or hard stool.
- **Next step:** Quantify the amount of blood loss and review vital signs; tachycardia is the initial sign of rapid blood loss. Hypotension is a late finding. Begin dietary changes and stool softeners; oral polyethylene glycolate is most commonly used and may be required for a few months to break the cycle of constipation. Parents should minimize foods known to be constipating (such as dairy products), increase water intake, and avoid bulking agents (such as fiber, psyllium).

## ANALYSIS

### *Objectives*

1. Know the differential diagnosis for rectal bleeding at various ages.
2. Know how to manage rectal bleeding.
3. Be familiar with methods of investigating the cause of bleeding.

### *Considerations*

The presentation of gastrointestinal (GI) tract bleeding will often depend on the site of bleeding and the rate of hemorrhage. Hematochezia usually indicates the site is in the large intestine, but if there is massive hemorrhage in

the small intestine, it may present similarly. Otherwise, bleeding in the small intestine tends to cause melena.

## APPROACH TO:

### **Rectal Bleeding**

## DEFINITIONS

**HEMATOCHEZIA:** Blood in the stool that is red or maroon-colored.

**MELENA:** Black tarry stools; color is produced when heme is oxidized by intestinal flora.

## CLINICAL APPROACH

While gastric and duodenal bleeding can cause nausea, vomiting, or diarrhea, other sites of hemorrhage in the intestinal tract rarely cause GI symptoms. Tachycardia and hypotension may be the first symptoms before hematochezia or melena follow. If there is any change in vital signs, immediate stabilization is necessary. Patients are admitted to the hospital for monitoring, and intravascular volume is initially restored with isotonic saline, then packed red blood cells may be needed. Frequent measurement of hemoglobin or hematocrit is indicated, and bleeding can be monitored in each stool via guaiac testing if blood is not grossly visible.

Laboratory evaluation for contributing coagulopathic conditions should be performed, which includes measurement of platelets, prothrombin time (PT), activated partial thromboplastin time (APTT), liver enzymes, and creatinine. Blood urea nitrogen (BUN) levels may be elevated due to urea being produced from hemoglobin breakdown in the GI tract. Investigation for an infectious cause, such as colitis or enteritis, should be undertaken if there is a history of fever or diarrhea.

X-rays are frequently used in neonates to look for signs of necrotizing enterocolitis (NEC), such as intramural air entering the portal venous system. In infants or children, a dilated portion of proximal bowel with air distally that outlines a telescoped portion signals intussusception. An obstructive pattern can also be seen with volvulus. Special imaging techniques include Meckel scan if Meckel diverticulum is suspected, ultrasound or air-contrast

enema for intussusception, angiography which also allows for embolization by an interventional radiologist, or a tagged red blood cell scan for low flow bleeds.

Pediatric gastroenterologists may be needed to identify the site or cause of the bleeding. The duodenum, stomach, and esophagus are evaluated with esophago-gastroduodenoscopy (EGD). Capsule endoscopy is a new tool that can be used to evaluate the small intestine. For lower GI bleeding, colonoscopy is performed once the patient is stabilized.

## COMPREHENSION QUESTIONS

- 12.1 A 2-month-old boy presents with his mom after having 3 days of stools with blood streaks intermixed in them. Over the past week, he has been stooling more often with an increase from 4 stools to 8 stools per day. He has been happy and afebrile, and no blood is found when she wipes him. He continues to take 3 ounces of standard infant formula at each feed. Which of the following statements about his condition is most accurate?
- A. He needs to be changed to soy formula.
  - B. Treatment will consist of changing him to an elemental formula, or if mom is breastfeeding, have her eliminate milk products from her diet.
  - C. Broad-spectrum antibiotics should be given for 10 days.
  - D. Provide reassurance that the condition is benign and transient and will resolve without any intervention.
  - E. There is usually a positive family history of lactose intolerance.
- 12.2 A 2-year-old girl presents with her second episode of bloody stool. Mom brings a diaper that is filled with brick-colored stool. The first episode had occurred 6 months ago and had improved over the course of a day, so no workup had been done. The child has had less appetite than usual for the day but no fever, vomiting, or complaints of pain. What would be the next steps in management?
- A. Prescribe a laxative and anti-hemorrhoid cream for 1 week and then follow-up if symptoms recur.

- B. Instruct mom to remove milk and milk products from her daughter's diet for 1 year, and then slowly re-introduce it.
- C. Inquire more about the amount of ibuprofen the girl has been taking and prescribe omeprazole.
- D. Admit the patient to the hospital for observation and Meckel scan.
- E. Ask mom about any family history of Crohn disease or ulcerative colitis, and send an erythrocyte sedimentation rate (ESR).

12.3 A 3-day-old girl is brought in to the emergency room (ER) by her parents after they noted blood-streaked stools. She has been feeding well; parents deny emesis and diarrhea. Which of the following components of the history would be *least* useful in determining the cause of the hematochezia?

- A. Ask the parents whether the baby was born at home or in the hospital.
- B. Review mom's records for the color of her amniotic fluid.
- C. Ask about the length of time it required for the patient to stool after birth and her specific number of stools.
- D. Ask if the baby was premature.
- E. Ask mom if she is breastfeeding and, if so, if she has any bleeding from the nipples.

12.4 A 15-month-old boy presents to the ER with two episodes of nonbilious vomiting. His dad reports that his son would not eat breakfast, was very fussy and irritable before the episodes began, appeared to have abdominal pain, but after the emesis, became calm and fell asleep. Two hours later, he awoke screaming and was inconsolable for about 30 minutes. He then fell back asleep. On your examination, the child awakens but lies quietly in his dad's arms. The abdominal and genitourinary examinations are normal. Guaiac of stool from the rectal exam is positive. What is the next best step in management?

- A. Consult a pediatric gastroenterologist and type and cross 5 cc/kg of packed red blood cells.
- B. Administer a dose of ceftriaxone and have patient follow-up with his pediatrician the day after for results of stool studies.
- C. Consult a pediatric surgeon and order an air-contrast enema.

- D. Measure the levels of *Helicobacter pylori* antibodies and administer omeprazole.
- E. Reassure dad that night terrors are common in this age group and may be provoked by an illness.

## ANSWERS

- 12.1 B.** Allergic proctocolitis is induced by allergy to the protein in cow's milk. Standard infant formulas are composed of this protein. Soy protein is similar in structure so cross-allergy often exists. The protein can cross over into breast milk. Elemental formulas are made of amino acids rather than complete proteins. If the inciting protein is not removed from the diet, the infant can progress to enterocolitis with resulting severe diarrhea, malabsorption, vomiting, and dehydration. The condition usually presents before 3 months of age and is more common in boys. There may be a family history of atopy.
- 12.2 D.** Meckel diverticulum is a pouch off the ileum due to a remnant of the omphalomesenteric duct. It is usually 3 to 6 cm in size and located 50 to 75 cm from the ileocecal valve. It is often lined with endothelium that has undergone meta-plastic change that simulates gastric mucosa; the acid that is secreted causes ulceration of the adjacent ileal mucosa. Symptoms of intermittent painless rectal bleeding usually appear at the age of 2 years. It produces 50% of all lower GI bleeds in children under the age of 2 years. A Meckel radionuclide scan is needed to confirm the diagnosis, but it has a high false-negative rate, so a diagnostic laparoscopy may be needed. Even if the bleeding stops, surgical excision of the mucosa is often done to prevent re-bleeding, obstruction, or diverticulitis.
- 12.3 D.** Necrotizing enterocolitis (NEC) occurs predominantly in preterm infants, with term infants accounting for less than 25% of the cases. Swallowed blood syndrome occurs on the 2nd to 3rd day of life. The blood may be from delivery or from the mother's nipple. The Apt test involves differentiating the fetal hemoglobin from maternal hemoglobin based on the infant's blood being alkali-resistant. Hemorrhagic disease of the newborn occurs in infants who do not receive vitamin K. The condition is usually not seen in newborns that are born in the hospital since intramuscular vitamin K is routinely given shortly after birth.

Hirschsprung disease presents with a delay in passing meconium after birth; it can progress to toxic megacolon and enterocolitis, which will present with bloody stools and even diarrhea.

- 12.4 C. Intussusception is the most common cause of intestinal obstruction in children under the age of 2 years. In most cases, a lead point is not identifiable, but the condition occurs when part of the small bowel telescopes into the lumen of a distal portion of bowel. The lumen of the inserted portion collapses and causes abdominal obstruction. Peristalsis is still active and attempts to propel contents past the obstruction; this creates episodes of severe colicky intermittent pain that on subsidence leave the patient calm or lethargic. This is a hallmark symptom of abdominal obstruction and requires a pediatric surgery consult. If the bowel wall becomes ischemic with resultant areas of necrosis, blood may appear, and this will usually be in the first 12 hours of the obstruction. Only 60% of infants will have the classic “currant jelly” stool composed of blood and mucus. An air-contrast enema can be diagnostic as well as therapeutic, but a pediatric surgeon should be available in case perforation occurs or if reduction is unsuccessful.

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### CLINICAL PEARLS

- Anal fissures are the most common cause of hematochezia in infants, children, and adolescents.
  - The differential diagnosis of hematochezia varies by age.
  - In newborns, the cause of hematochezia is most often a life-threatening condition, whereas the etiology in infants and children is more often benign.
  - If the patient is ill-appearing and there is no visible anal fissure, further investigation with stool studies, laboratory, or imaging is indicated.
  - Tachycardia is the first indication that the rate or volume of bleeding is significant and warrants admission to the hospital.
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A 4-year-old child complains of ear pain. He has a temperature of 102.1°F (38.9°C) and has had a cold for several days, but he has been eating well and his activity has been essentially normal.

- ▶ What is the most likely diagnosis?
- ▶ What is the best therapy?

### ANSWERS TO CASE 13: **Acute Otitis Media**

*Summary:* A preschool child presents with ear pain and fever.

- **Most likely diagnosis:** Acute otitis media (AOM)
- **Best therapy:** Oral antibiotics

## ANALYSIS

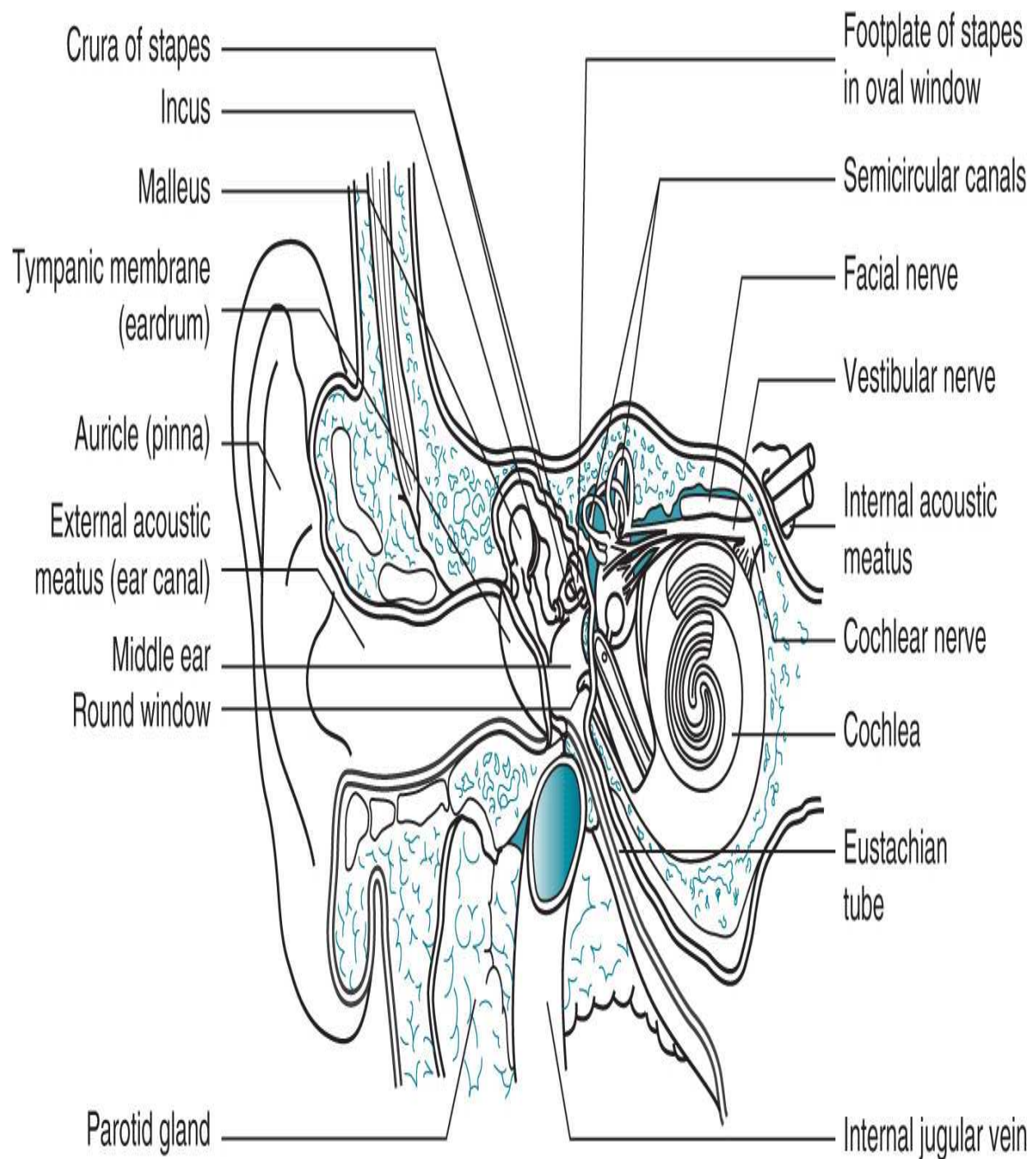
### *Objectives*

1. Be familiar with the epidemiology of otitis media (OM) in children.
2. Understand the treatment of this condition.
3. Learn the consequences of severe infection.

### *Considerations*

Otitis media is high on the differential diagnosis for this child with upper respiratory infection (URI) and ear pain. The diagnosis can be confirmed by pneumatic otoscopy and treatment started. A “telephone diagnosis” should be avoided. [Figure 13-1](#) illustrates the anatomy of the middle ear.





**Figure 13-1.** Anatomy of the middle ear. (Redrawn, with permission, from Rudolph CD, Rudolph AM, Hostetter MK, Lister G, Siegel NJ, eds. *Rudolph's Pediatrics*. 21st ed. New York, NY: McGraw-Hill; 2003:1240.)

APPROACH TO:

**Acute Otitis Media**

## DEFINITIONS

**ACUTE OTITIS MEDIA (AOM):** A condition of otalgia (ear pain), fever, and other symptoms along with findings of a red, opaque, poorly moving, bulging tympanic membrane (TM).

### MYRINGOTOMY AND PLACEMENT OF PRESSURE

**EQUALIZATION TUBES:** A surgical procedure involving TM incision and placement of pressure equalization (PE) tubes (tiny plastic or metal tubes anchored into the TM) to ventilate the middle ear and help prevent reaccumulation of middle ear fluid.

**OTITIS MEDIA WITH EFFUSION:** A condition in which fluid collects behind the TM but without signs and symptoms of AOM. Sometimes also called serous OM.

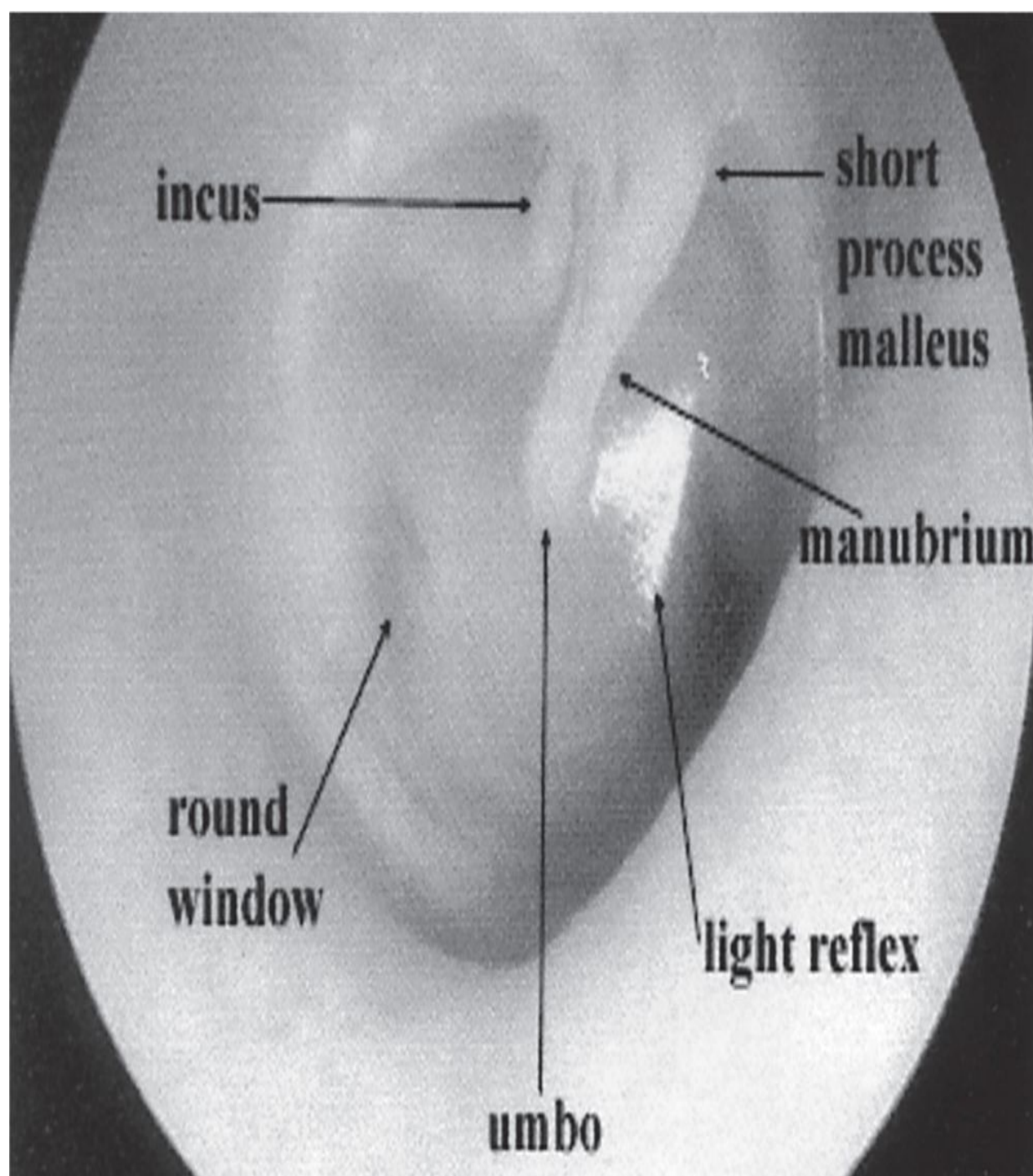
**PNEUMATIC OTOSCOPY:** The process of obtaining a tight ear canal seal with a speculum and then applying slight positive and negative pressure with a rubber bulb to verify TM mobility.

**TYMPANOCENTESIS:** A minor surgical procedure in which a small incision is made into the TM to drain pus and fluid from the middle ear space. This procedure is rarely done in the primary care office, but rather is done by the specialist.

## CLINICAL APPROACH

Otitis media is a common childhood diagnosis. **Common bacterial pathogens include *Streptococcus pneumoniae*, nontypeable *Haemophilus influenzae*, and *Moraxella catarrhalis*.** Other organisms, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, are seen in neonates and patients with immune deficiencies. Viruses can cause AOM, and in many cases the etiology is unknown. Acute OM is diagnosed in a child with fever (usually  $<104^{\circ}\text{F}$  [ $40^{\circ}\text{C}$ ]), ear pain (often nocturnal, awakening child from sleep), and generalized malaise. Systemic symptoms may include anorexia, nausea, vomiting, diarrhea, and headache. Examination findings include a **red, bulging TM that does not move well with pneumatic otoscopy.** The TM may be opaque with pus behind it, the middle ear landmarks may be obscured, and, if the TM has

ruptured, pus may be seen in the ear canal. Normal landmarks are shown in Figure 13-2.



**Figure 13-2.** The tympanic membrane. (Reproduced, with permission, from Rudolph CD, Rudolph AM, Hostetter MK, Lister G, Siegel NJ, eds. *Rudolph's Pediatrics*. 21st ed. New York, NY: McGraw-Hill; 2003:1240.)

In some situations and in a child with few symptoms, a “watchful waiting” period of a few days may be indicated since many AOM cases self-resolve. Should antibiotics be deemed necessary and depending on a community’s bacterial resistance patterns, amoxicillin at doses up to 80 to 90 mg/kg/d for 7 to 10 days is often the initial treatment. If clinical failure is noted after 3 treatment days, a change to amoxicillin-clavulanate, cefuroxime axetil, azithromycin, cefixime, ceftriaxone, or tympanocentesis is considered. Adjuvant therapies (analgesics or antipyretics) are often indicated, but other measures (antihistamines, decongestants, and corticosteroids) are ineffective.

**After an AOM episode, middle ear fluid can persist for up to several months.** If hearing is normal, middle ear effusion often is treated with observation; some practitioners treat with antibiotics. **When the fluid does not resolve or recurrent episodes of suppurative OM occur, especially if hearing loss is noted, myringotomy with PE tubes is often implemented.**

Rare but serious OM **complications** include **mastoiditis, temporal bone osteomyelitis, facial nerve paralysis**, epidural and subdural abscess formation, meningitis, lateral sinus thrombosis, and otitic hydrocephalus (evidence of increased intracranial pressure with OM). An AOM patient whose clinical course is unusual or prolonged is evaluated for one of these conditions.

## COMPREHENSION QUESTIONS

- 13.1 An 8-year-old boy has severe pain with ear movement. He has no fever, nausea, vomiting, or other symptoms. He has been in good health, having just returned from summer camp where he swam, rode horses, and water-skied. Ear examination reveals a somewhat red pinna that is extremely tender with movement, a very red and swollen ear canal, but an essentially normal TM. Which of the following is the most appropriate next course of therapy?
- A. Administration of topical mixture of polymyxin and corticosteroids
  - B. High-dose oral amoxicillin
  - C. Intramuscular ceftriaxone
  - D. Intravenous vancomycin
  - E. Tympanocentesis and culture

- 13.2 Three days after beginning oral amoxicillin therapy for OM, a 4-year-old boy has continued fever, ear pain, and swelling with redness behind his ear. His ear lobe is pushed superiorly and laterally. He seems to be doing well otherwise. Which of the following is the most appropriate course of action?
- A. Change to oral amoxicillin-clavulanate
  - B. Myringotomy and parenteral antibiotics
  - C. Nuclear scan of the head
  - D. Topical steroids
  - E. Tympanocentesis
- 13.3 A 5-year-old girl developed high fever, ear pain, and vomiting a week ago. She was diagnosed with OM and started on amoxicillin-clavulanate. On the third day of this medication she continued with findings of OM, fever, and pain. She received ceftriaxone intramuscularly and switched to oral cefuroxime. Now, 48 hours later, she has fever, pain, and no improvement in her OM; otherwise she is doing well. Which of the following is the most logical next step in her management?
- A. Addition of intranasal topical steroids to the oral cefuroxime
  - B. Adenoidectomy
  - C. High-dose oral amoxicillin
  - D. Oral trimethoprim-sulfamethoxazole
  - E. Tympanocentesis and culture of middle ear fluid
- 13.4 A 1-month-old boy has a fever to 102.7°F (39.3°C), is irritable, has diarrhea, and has not been eating well. On examination he has an immobile red TM that has pus behind it. Which of the following is the most appropriate course of action?
- A. Admission to the hospital with complete sepsis evaluation
  - B. Intramuscular ceftriaxone and close outpatient follow-up
  - C. Oral amoxicillin-clavulanate
  - D. Oral cefuroxime
  - E. High-dose oral amoxicillin



# ANSWERS

- 13.1 **A.** The patient likely has an otitis externa that was caused by his swimming (also known as swimmer's ear). Treatment is the application of a topical agent as described. Insertion of a wick may assist in excess fluid absorption in the macerated, swollen, and occluded ear canal. Causative organisms include *Pseudomonas* species (or other gram-negative organisms), *S aureus*, and occasionally fungus (*Candida* or *Aspergillus* species).
- 13.2 **B.** The child has mastoiditis, a clinical diagnosis that can require computed tomography scan confirmation. Treatment includes myringotomy, fluid culture, and parenteral antibiotics. Surgical drainage of the mastoid air cells may be needed if improvement is not seen in 24 to 48 hours.
- 13.3 **E.** After failing several antibiotic regimens, tympanocentesis and culture of the middle ear fluid are indicated.
- 13.4 **A.** Very young children with OM (especially if irritable or lethargic) are at higher risk for bacteremia or other serious infection. Hospitalization and parenteral antibiotics often are needed.
- 

## CLINICAL PEARLS

- The most common bacterial pathogens causing otitis media (OM) are *S pneumoniae*, nontypeable *H influenzae*, and *M catarrhalis*.
- Examination findings of OM include a red, bulging tympanic membrane that does not move well with pneumatic otoscopy, an opaque tympanic membrane with pus behind it, obscured middle-ear landmarks, and, if the tympanic membrane has ruptured, pus in the ear canal.
- Initial treatment of OM often includes amoxicillin (depending on local bacterial resistance patterns). If a clinical failure is seen on day 3, a change to amoxicillin-clavulanate, cefuroxime axetil, ceftriaxone, or a tympanocentesis is indicated.
- Complications are rare but include mastoiditis, temporal bone osteomyelitis, facial nerve palsy, epidural and subdural abscess formation, meningitis, lateral sinus thrombosis, and otitic hydrocephalus.

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You are called to the delivery room because a now 2-minute-old male was born floppy and blue; his Apgar scores were 4 and 5. He has not responded well to stimulation and blow-by oxygen. The obstetrician who is resuscitating the infant informs you that the child was born by a spontaneous vaginal delivery to a 24-year-old primagravida parity 1 woman. Her pregnancy was uncomplicated. Fetal heart tones were stable throughout the labor. Spinal epidural anesthesia was administered but was only partially effective; the obstetrician supplemented her labor analgesia with intravenous meperidine (Demerol) and promethazine (Phenergan). The amniotic fluid was not meconium stained, and the mother had no evidence of intraamniotic infection.

► What is the next step?

### ANSWER TO CASE 14: Neonatal Resuscitation

*Summary:* A newborn is born floppy, blue, and has responded poorly to initial resuscitation efforts of warming, drying, and stimulation.

- **Next step:** Evaluate heart rate (HR) and respirations. If no respirations are found or if HR is less than 100 bpm (beats/min), initiate positive-pressure ventilation (PPV) by bag and mask. Because this mother received meperidine during the labor process, naloxone (Narcan) administration is an important step in resuscitation.

## ANALYSIS

### *Objectives*

1. Understand the steps of newborn delivery room resuscitation.
2. Become familiar with use of the Apgar score.
3. Become familiar with conditions causing newborn transition problems.

### *Considerations*

This depressed infant was born to a healthy mother without prenatal or delivery complications other than the partially effective epidural anesthesia, which was supplemented with meperidine and promethazine. PPV was



initiated and naloxone administered. The provider must appreciate the timing of maternal meperidine administration and its continued effects on the neonate.

APPROACH TO:

**Neonatal Resuscitation**

## DEFINITIONS

**NARCOSIS:** The condition of deep stupor or unconsciousness produced by a chemical substance such as a drug or anesthesia.

**PERINATAL HYPOXIA:** Inadequate oxygenation of a neonate that, if severe, can lead to brainstem depression and secondary apnea unresponsive to stimulation.

**POSITIVE-PRESSURE VENTILATION (PPV):** Mechanically breathing using a bag and mask.

## CLINICAL APPROACH

Delivery room resuscitation follows the **ABC** rules of resuscitation for patients of all ages: establish and maintain the **Airway**, control the **Breathing**, and maintain the **Circulation** with medications and chest compressions (if necessary).

In this case, the meperidine given during labor probably is responsible for the infant's apnea and poor respiratory effort. Neonates with narcosis usually have a good HR response but poor respiratory effort in response to bag-and-mask ventilation. **The therapy for narcotic-related depression** is intravenous (IV), intramuscular (IM), subcutaneous (SQ), or endotracheal administration of **naloxone** (Narcan); repeated doses may be required should respiratory depression recur.

The **Apgar score** ([Table 14-1](#)) is widely used to evaluate a neonate's transition from the intra- to extrauterine environment. Scores of 0, 1, or 2 are given at 1 and 5 minutes of life for the listed signs. The 1-minute score helps to determine an infant's well-being in the period just prior to delivery, and scores less than 3 historically have been used to indicate the need for

immediate resuscitation. In current practice, HR, color, and respiratory rate (RR) rather than the 1-minute Apgar score are used to determine this need. The 5-minute score is one indicator of how successful the resuscitation efforts were. Some continue to measure Apgar scores beyond the 5-minute period to determine the continued response to resuscitation efforts. The Apgar score alone cannot determine neonatal morbidity or mortality.

Sign	0	1	2
Heart rate	Absent	<100 bpm	>100 bpm
Respiratory effort	Absent	Slow, irregular	Good, crying
Muscle tone	Limp	Some flexion of extremities	Flexed, active motion
Reflex irritability (response to catheter in nose)	No response	Grimace	Cough or sneeze
Color	Blue, pale	Body pink, acrocyanosis (extremities blue)	Completely pink

**Table 14-1 • APGAR EVALUATION OF A NEWBORN**

## COMPREHENSION QUESTIONS

**14.1** A female infant is born through emergency cesarean section to a 34-year-old mother whose pregnancy was complicated by hypertension and abnormal fetal heart monitoring. At delivery she is covered in thick, green meconium and is limp, apneic, and bradycardic. Which of the following is the best first step in her resuscitation?

A. Administer IV bicarbonate.

- B. Administer IV naloxone.
- C. Initiate bag-and-mask ventilation.
- D. Initiate chest compressions immediately.
- E. Intubate with an endotracheal tube and suction meconium from the trachea.

14.2 A term male is delivered vaginally to a 22-year-old mother. Immediately after birth he is noted to have a scaphoid abdomen, cyanosis, and respiratory distress. Heart sounds are heard on the right side of the chest, and the breath sounds seem to be diminished on the left side. Which of the following is the most appropriate next step in his resuscitation?

- A. Administer IV bicarbonate.
- B. Administer IV naloxone.
- C. Initiate bag-and-mask intubation.
- D. Initiate chest compressions immediately.
- E. Intubate with an endotracheal tube.

14.3 A 37-week-gestation male is born after an uncomplicated pregnancy to a 33-year-old mother. At birth he was lethargic and had an HR of 40. Oxygen was administered via bag and mask, and he was intubated; his HR remained at 40 bpm. Which of the following is the most appropriate next step?

- A. Administer IV bicarbonate.
- B. Administer IV atropine.
- C. Administer IV epinephrine.
- D. Administer IV calcium chloride.
- E. Begin chest compressions.

14.4 A term female infant is born vaginally after an uncomplicated pregnancy. She appears normal but has respiratory distress when she stops crying. When crying she is pink; when not she makes vigorous respiratory efforts but becomes dusky. Which of the following is the likely explanation for her symptoms?

- A. Choanal atresia

- B. Diaphragmatic hernia
- C. Meconium aspiration
- D. Neonatal narcosis
- E. Pneumothorax

## ANSWERS

- 14.1 E. An attempt is made to remove the meconium from the oropharynx and the airway prior to initiation of respirations. Ideally, the obstetrician will begin suctioning the meconium upon delivery of the head, and the pediatrician will further remove meconium with an aspirator or through endotracheal intubation with suction. Ventilation is initiated after meconium is removed. The goal is to remove airway meconium and to prevent its aspiration into the small airways where ventilation-perfusion mismatch may occur with deleterious effects.
- 14.2 E. The case describes diaphragmatic hernia. As a result of herniated bowel in the chest, these children often have pulmonary hypoplasia. Bag-and-mask ventilation will cause accumulation of bowel gas (which is located in the chest) and further respiratory compromise. Therefore, endotracheal intubation is the best course of action.
- 14.3 E. If the HR is still less than 60 bpm despite PPV with 100% oxygen, then chest compressions are given for 30 seconds. If the HR is still less than 60 bpm, then drug therapy (usually epinephrine) is indicated.
- 14.4 A. Infants are obligate nose breathers until about 4 months of age. When crying they can breathe through their mouth, but they must have a patent nose when quiet. Choanal atresia is identified by passing a feeding tube through each nostril or by identification of clouding on cold metal held under the infant's nose. Should choanal atresia be diagnosed, endotracheal intubation bypasses the airway obstruction until surgical repair can be completed.

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## CLINICAL PEARLS

- An infant with slow heart rate, poor color, and inadequate respiratory effort requires immediate resuscitation.

- The therapy for narcosis (newborn respiratory depression because of maternal pain control) is intravenous, intramuscular, subcutaneous, or endotracheal administration of naloxone (Narcan).
  - A child with diaphragmatic hernia often presents with immediate respiratory distress, scaphoid abdomen, cyanosis, and heart sounds displaced to the right side of the chest.
  - Choanal atresia results in respiratory distress when a child stops crying; immediate treatment is intubation until surgical correction can be completed.
- 

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## CASE 15

A 12-month-old boy whom you have followed since birth arrives for a well-child visit. The mother is concerned that the baby's manner of crawling, where he drags his legs rather than using a four-limbed movement, is abnormal. She says that the child only recently began crawling and he does not pull to a stand. You noted at his 6-month visit that he was not yet rolling over or sitting; previous visits were unremarkable as was the mother's pregnancy and vaginal delivery. On examination today, you note that he positions his legs in a "scissoring" posture (ie, legs extended and crossed) when held by the axillae.

- ▶ What is the initial step in the evaluation of this child?
- ▶ What is the most likely diagnosis?
- ▶ What is the next step in the evaluation?

### ANSWERS TO CASE 15: **Cerebral Palsy**

*Summary:* A 12-month-old boy crawls using primarily his upper extremities, and holds his legs in a "scissoring" posture when suspended.

- **Initial step:** Gather detailed history, focusing on the age at which developmental milestones were achieved; obtain thorough pregnancy, birth, social, and family histories; and perform a detailed neurologic examination.
- **Most likely diagnosis:** Cerebral palsy (CP).
- **Next step:** Vision and hearing testing, consider a brain magnetic resonance imaging (MRI) scan, and arrange for therapy with a developmental specialist.

## ANALYSIS

## ***Objectives***

1. Know the definition of CP.
2. Recognize the classifications of CP.
3. Know the basic therapeutic approach to CP.

## ***Considerations***

The spasticity of the baby's lower extremities described is abnormal and is suggestive of CP. He has gross motor delay. A complete developmental and neurologic assessment is crucial for initiating therapies that will help him achieve maximal functional outcome. Although often of low yield, an attempt should be made to identify the etiology of the child's CP. Knowing the etiology can aid in developing a treatment plan, subsequent family planning (especially if the etiology is inherited), and assuaging parental guilt for this child's condition.

APPROACH TO:

**Cerebral Palsy**

## **DEFINITIONS**

**CEREBRAL PALSY (CP):** A disorder of nonprogressive movement and posture that results from an insult to or anomaly of the developing central nervous system (CNS). This definition recognizes the central origin of the dysfunction, thus distinguishing it from neuropathies and myopathies.

**DEVELOPMENTAL DELAY:** Failure of a child to reach developmental milestones of gross motor, fine motor, language, or social-adaptive skills at anticipated ages.

**NEUROLOGIC DEFICIT:** Abnormal functioning or lack of function of a part of the nervous system.

## **CLINICAL APPROACH**

With a prevalence of 3 to 4 cases per 1000 live births, **CP is the most common childhood movement disorder. Approximately one-third of CP patients also have seizures, and approximately 60% are mentally**

**retarded.** Deafness, visual impairments, swallowing difficulty with concomitant aspiration, limb and sensory impairments, and behavioral disturbances are common comorbidities.

Most children with CP have no identifiable risk factors. **Current research indicates that CP most likely is the result of antenatal insults.** Subsequent difficulties during the **pregnancy, delivery, and perinatal period** are thought to reflect these insults and are **probably not the primary cause of CP.**

Cerebral palsy, or “static” encephalopathy, is the result of a one-time CNS insult. In contrast, progressive encephalopathies destroy brain function with time. The term *static* is misleading, however, because the manifestations of CP may change with age. Contractures and postural deformities may become more severe with time or may improve with therapy. Also, a child’s changing developmental stages early in life can alter the expression of his or her neurologic deficits.

Immaturity of the CNS at birth makes diagnosis of CP nearly impossible in a neonate. If a CNS insult is suspected, head imaging (by ultrasound or MRI) can be helpful in recognizing CP early. Possible imaging findings include periventricular leukomalacia, atrophy, or focal infarctions. Beyond infancy, CP is suspected when a child fails to meet anticipated developmental milestones.

Examples of concerning findings are:

- A stepping response after the age of 3 months
- A Moro reflex beyond 6 months
- An asymmetrical tonic neck reflex beyond 6 months

Cerebral palsy can be classified in terms of physiologic, topographic, or functional categories. Physiologic descriptors identify the major motor abnormality and are divided into pyramidal (spastic) and extrapyramidal (nonspastic) categories. Extrapyramidal types can be subdivided further into choreoathetoid, ataxic, dys-tonic, or rigid types.

The topographic classification categorizes CP types according to limb involvement. **Hemiplegia** refers to involvement of a single lateral side of the body, with greater impairment of the upper extremities than the lower extremities. **Diplegia** describes four-limb involvement, with greater



impairment of the lower extremities. **Spastic quadriplegia** is four-limb involvement with significant impairment of all extremities, although the upper limbs may be less impaired than lower limbs. (The term *paraplegia* is reserved for spinal and lower motor neuron disorders.)

The functional classification of CP relies on the “motor quotient” to place patients into minimal, mild, moderate, and severe (profound) categories. The motor quotient is derived by dividing the child’s “motor age” (ie, motor skills developmental age) with the chronologic age. A motor quotient of 75 to 100 represents minimal impairment, 55 to 70 mild impairment, 40 to 55 moderate impairment, and lesser quotients severe impairment. These categories help clinicians identify children with less obvious impairments so that early treatment can be provided.

The evaluation of CP is based on the history and physical examination. The yield of diagnostic findings with brain imaging and metabolic or genetic testing is low but can be helpful in managing the patient, in future family planning, and in reassuring the parents. Identification of comorbid conditions includes cognitive testing for mental retardation and electroencephalography (EEG) for seizures.

Treatment goals include maximizing motor function and preventing secondary handicaps. During the preschool years, the child’s communication ability is important. School performance and peer acceptance become important issues for older children. Physical therapy for motor deficits may be supplemented with pharmacologic and surgical interventions. Occupational therapy improves positioning and allows for better interaction with the environment and eases care as the child grows. The family’s psychological and social needs should not be overlooked; children may require extensive physical and emotional support.

## COMPREHENSION QUESTIONS

- 15.1 A term infant requires resuscitation after a spontaneous vaginal delivery. The Apgar scores at 1, 5, and 10 minutes were 2, 7, and 9, respectively. The mother’s medical records show that she received routine prenatal care with normal prenatal ultrasonogram, triple screen, and glucose tolerance tests. The nurse tells you that the father seemed very agitated and mentioned “suing the obstetrician if the baby does not turn out

normal.” Your examination of the baby reveals no abnormalities. In counseling the family, which of the following is most appropriate?

- A. Inform them that your examination findings indicate that everything is fine.
- B. Tell them that the low Apgar scores at 1 and 5 minutes indicate that the baby suffered perinatal asphyxia.
- C. Inform them that because the pregnancy was uncomplicated, any neurologic deficit that the baby may develop likely can be attributed to events occurring at delivery.
- D. Tell them that your examination findings are reassuring, and that you will perform a careful developmental assessment at every well-child visit.
- E. Avoid speaking to the parents until you have had a chance to speak with the obstetrician and to see the cord blood gas results.

15.2 A 4-year-old child with CP comes to your clinic for the first time for a routine visit. He walks with the help of leg braces and a walker, and his speech is slurred and limited to short phrases. He has never been hospitalized, and he does not have swallowing problems. He began walking at the age of 2.5 years, and he is unable to take off his clothes and use the toilet without help. On examination you find that the boy has only minimally increased tone in the upper extremities but good fine motor coordination; he has significantly increased tone and deep tendon reflexes in the lower extremities. How would you categorize this child’s CP?

- A. Mild, diplegic
- B. Mild, hemiplegic
- C. Moderate, diplegic
- D. Moderate, quadriplegic
- E. Severe, diplegic

15.3 A female is born through spontaneous vaginal delivery at 28-week gestation because of an incompetent cervix. Which of the following features of her clinical course in the neonatal intensive care unit (ICU) is most likely to correlate with her clinical outcome 5 years from now?

- A. Administration of surfactant
- B. Apnea of prematurity
- C. Grade IV intraventricular hemorrhage
- D. Retinopathy of prematurity stage 1 on initial ophthalmologic examination
- E. Umbilical artery catheterization

**15.4** The parents of a 2-year-old girl, recent immigrants from Guatemala, bring their child to you for the first time. The child was born at term after an uncomplicated pregnancy and delivery, and her neonatal course was uneventful. She sat without support at 6 months of age, pulled to a stand at 10 months, and walked at 14 months. She has a 10-word vocabulary, is able to drink from a cup, and feeds herself with a spoon. A previous child in the family died at the age of 5 years from “heart trouble.” On physical examination, you note lower extremity contractures, hand stiffness, somewhat coarse facial features, and hepatosplenomegaly. The child’s growth is within normal limits, and her examination is otherwise normal. Which of the following is the most appropriate next step to diagnose this child’s condition?

- A. Abdominal computerized tomography (CT)
- B. Brain magnetic resonance imaging (MRI)
- C. Chromosomal analysis
- D. Tests for a storage disorder
- E. Thyroid function studies

## ANSWERS

**15.1 D.** The Apgar score at 1 minute reflects the neonatal environment immediately prior to birth; the 5-minute score correlates the infant’s response to resuscitation. The Apgar scores are not an accurate reflection of morbidity. An examination is a better indicator of the child’s outcome, but CP cannot be ruled out on the basis of a normal neonatal physical examination. A discussion of the events of delivery is best left to the obstetrician; the majority of difficult deliveries are the result of a previously unidentified antenatal insult. However, avoidance of the

parents will likely only further their anxiety and may impede your efforts to provide care for the child.

- 15.2 C. In diplegia all four extremities are affected, with greater impairment of the lower extremities. As most children walk by the age of 14 months, this child's motor quotient is  $14 \text{ months} / 30 \text{ months} = 0.47$ , which classifies him as moderately impaired.
- 15.3 C. Intraventricular hemorrhage is a complication in preterm infants. It is associated with seizures, hydrocephalus, and periventricular leukomalacia. A grade IV bleed involves the brain parenchyma, putting this child at higher risk for neurodevelopmental handicap.
- 15.4 D. The enlarged liver and spleen, the coarse facies, and the history of a previous child's death from "heart trouble" point to a storage disorder. Her joint contractures and hand stiffness may be explained by an abnormal metabolism rather than a CNS deficit as in CP.
- 

### CLINICAL PEARLS

- Cerebral palsy is a disorder of movement or posture resulting from an insult to, or an anomaly of, the central nervous system.
  - Most children with cerebral palsy have no identifiable risk factors for the disorder.
  - Optimal treatment plans for cerebral palsy use a multidisciplinary approach.
- 

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## CASE 16

A 5-year-old girl comes to your clinic for the first time with complaints of fever, malaise, and increased cough for 2 days. She has a history of asthma for which she uses a steroid inhaler daily and an albuterol inhaler as needed. She has been tried on various over-the-counter cold and allergy remedies, but her respiratory symptoms have been worsening over the past several months with an almost daily cough, and sometimes she expectorates blood-tinged mucus. Her past medical history is notable for an episode of rectal prolapse and “sinusitis” during each of the past two winter seasons. Her mother also reports that her daughter has “always been small for her age.” Your examination reveals a moderately ill-appearing child whose height and weight are at the 5th percentile for age. Her temperature is 101°F (38.3°C) and respiratory rate is 32 breaths/min. She has scant purulent rhinorrhea bilaterally, wheezes in all lung fields, and diminished breath sounds on the right side. Heart sounds and capillary refill are normal, yet she has digital clubbing.

- ▶ What is the diagnostic approach in the evaluation of this child?
- ▶ What is the most likely diagnosis?
- ▶ What is the next step in evaluation?

### ANSWERS TO CASE 16: Cystic Fibrosis

*Summary:* A small-appearing, 5-year-old girl previously diagnosed with asthma, rectal prolapse, and sinusitis presents with fever, scant purulent rhinorrhea, abnormal breath sounds, and digital clubbing.

- **Diagnostic approach:** Gather perinatal, past medical, family, and dietary histories, newborn screen results, and a thorough systems review. Plot the child’s height and weight on a standard growth curve.
- **Most likely diagnosis:** Cystic fibrosis (CF).
- **Next step in evaluation:** Obtain a chest radiograph and perform a sweat chloride test.

# ANALYSIS

## *Objectives*

1. Know the historical clues and physical signs to distinguish CF from more common conditions.
2. Know how to accurately diagnose CF.
3. Have a basic understanding of the implications and limitations of genetic testing for CF.

## *Considerations*

A careful review of this child's frequency and severity of respiratory symptoms, response to medications, and general health is warranted. Her small size and digital clubbing (unusual findings for asthma) suggest alternative diagnoses for her respiratory problems. Recurrent sinusitis is uncommon in young children because their nasal passages are not fully pneumatized; this girl likely was incorrectly diagnosed or has an underlying, predisposing condition for this problem.

APPROACH TO:

**Cystic Fibrosis**

# DEFINITIONS

**CLUBBING:** Increase in the angle between the nail and nail base of 180° or greater, and softening of the nail base to palpation. Although the condition can be familial, clubbing is uncommon in children, usually indicating chronic pulmonary, hepatic, cardiac, or gastrointestinal disease.

**CYSTIC FIBROSIS (CF):** The major cause of chronic debilitating pulmonary disease and pancreatic exocrine deficiency in the first three decades of life. It is characterized by the triad of chronic obstructive pulmonary disease, pancreatic exocrine deficiency, and abnormally high sweat electrolyte concentrations. Characteristic pancreatic changes give the disease its name.

# CLINICAL APPROACH

Cystic fibrosis (CF) afflicts 1 of 3500 whites, 1 of 15,000 African Americans, 1 of 9200 Hispanics, and 1 of 32,100 Asian Americans. It almost always involves the **respiratory tract**; most patients develop **bronchiectasis** by the age of 18 months, although some may not experience respiratory difficulty for several years. Children are commonly misdiagnosed as asthmatic, but a careful history and physical examination ultimately demonstrates clues of CF. **Persistent bronchial obstruction from impaired mucus secretion and damage to the respiratory cilia** predisposes patients to secondary bacterial infection, which leads to a cycle of inflammation, tissue damage, further obstruction, and chronic infection. **Bacterial pneumonia** is initially caused by *Staphylococcus aureus*, and then by *Pseudomonas aeruginosa*. Most patients with advanced disease harbor **heavy, slime-producing mucoid** variants of *Pseudomonas aeruginosa*, rarely found in other conditions. Once established, these bacteria are virtually impossible to eradicate.

Airway reactivity is present in 50% of patients, but bronchodilator response is unpredictable and varies. Pneumothorax, hemoptysis, and *cor pulmonale* are frequent complications with advanced disease; pulmonary problems ultimately cause respiratory and cardiac failure. Clubbing and hypertrophic osteoarthropathy signal the underlying organ dysfunction. Chronic nasal congestion and sinus opacification are common, but acute sinusitis occurs infrequently. Children with CF may develop nasal polyps, with resultant nasal obstruction, headaches, and mouth breathing.

**Children with CF grow poorly because of maldigestion from exocrine pancreatic insufficiency.** This can lead to abdominal distention, **rectal prolapse**, minimal subcutaneous fat and muscle mass, and frequent passage of oily, malodorous, floating stools. The resulting fat-soluble vitamin deficiencies may manifest as peripheral neuropathy and hemolytic anemia (vitamin E), night blindness (vitamin A), or mucosal bleeding (vitamin K). If glands become distended with secretions or the intestinal lumen is filled with inspissated material, **meconium ileus** or intestinal obstruction can occur.

**Fatty liver infiltration or focal biliary cirrhosis** appears in many CF patients. Hepatomegaly, esophageal varices, and hypersplenism caused by portal hypertension develop in a small proportion of teens, while cholelithiasis is common in adults. In neonates, the blocked intrahepatic bile ducts may cause prolonged conjugated jaundice. Other symptoms are



**azoospermia**, endocervicitis, enlarged salivary glands, and a “salty taste” on the skin (due to eccrine sweat gland dysfunction). Patients and their families require extensive psychosocial support.

The diagnosis of CF is usually based on a positive sweat test in conjunction with one of the following: typical chronic obstructive pulmonary disease, documented exocrine pancreatic insufficiency, and/or a positive family history. Persons with CF have **elevated sweat electrolyte concentrations because of abnormalities in the CF transmembrane conductance regulator (CFTR) protein**. Appropriate technique is important when attempting to measure sweat chloride in infants, in whom the collection of an adequate sweat quantity may be difficult. Elevated sweat electrolyte levels (false positives) have been reported in conditions such as anorexia nervosa, hypothyroidism, and nephrogenic diabetes insipidus. False-negative results can occur in CF patients with edema and hypoproteinemia. Because the implications of false test results are great, sweat testing is most appropriately obtained when a reasonable clinical suspicion of CF exists (see [Table 16-1](#) for indications) and repeated when the initial test results are in doubt.

## Gastrointestinal

Chronic diarrhea

Steatorrhea

Meconium ileus or plug syndrome

Rectal prolapse

Cirrhosis/portal hypertension

Prolonged neonatal jaundice

Pancreatitis

Deficiency of fat-soluble vitamins (especially A, E, K)

## Respiratory Tract

### Upper

- Nasal polyps
- Pansinusitis on radiographs

### Lower

- Chronic cough
- Recurrent “wheezing” bronchiolitis
- Recurrent or intractable asthma
- Obstructive pulmonary disease
- Staphylococcal pneumonia
- *Pseudomonas aeruginosa* (especially mucoid) from throat, sputum, or bronchoscopy cultures

## Other

Digital clubbing

Family history of cystic fibrosis

Failure to thrive

Hyponatremic, hypochloremic alkalosis

Severe dehydration or heat prostration incompatible with history

“Tastes salty”

Male infertility

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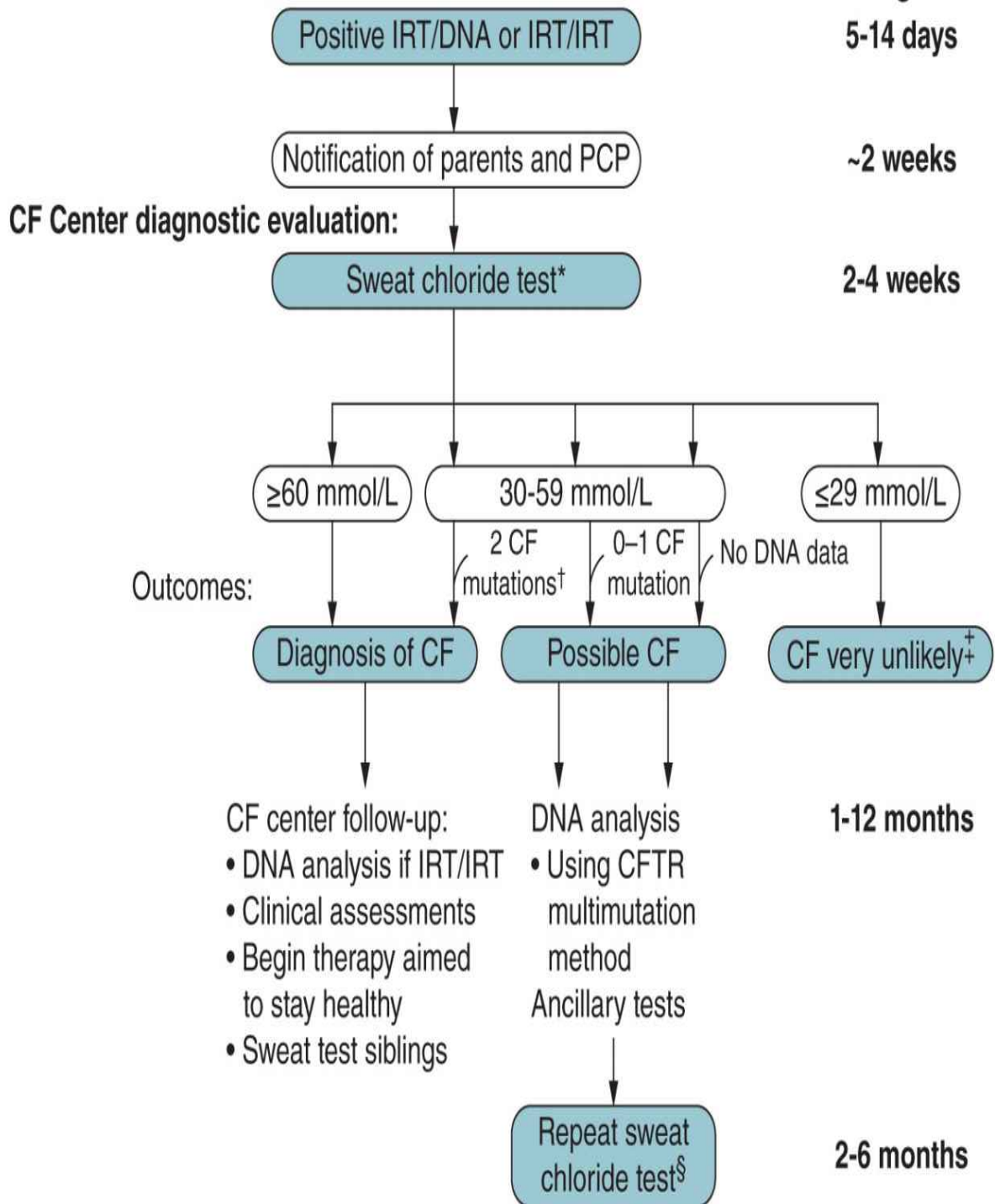
### Table 16-1 • INDICATIONS FOR SWEAT TESTING

**DNA testing** may be used when CF is suspected but the results of sweat testing are negative or equivocal. Disease is caused by mutations in the **long arm of chromosome 7**, the most common being a single phenylalanine deletion at **amino acid 508 ( $\Delta$  508)**. Available tests detect that more than 90% of individuals carry two CF gene mutations, but some children have only one or no detectable mutations by this methodology. The disease shows **autosomal recessive** inheritance.

Because research demonstrates that newborn screening improves nutritional status and growth and reduces hospitalizations, routine testing for CF is now performed for all newborns in the United States. The blood spot screening test detects the pancreatic enzyme immunoreactive trypsinogen (IRT), which is elevated in infants with CF. Second-tier testing for samples with high IRT levels relies on a second IRT test or limited DNA testing.

Infants with positive results on the newborn screen undergo sweat chloride testing for definitive confirmation. False-negative results are possible with the IRT newborn screen, so infants with symptoms suggestive of CF (such as meconium ileus) should undergo further testing even if newborn screen results are negative ([Figure 16-1](#)).

## CF Newborn screening result:



\* If the baby is at least 2 kg and more than 36 weeks gestation at birth, perform bilateral sweat sampling/analysis with either Gibson-Cooke or Macroduct® method; repeat as soon as possible if sweat quantity is less than 75 mg or 15 µl, respectively.

<sup>†</sup> CF mutation refers to a CFTR mutant allele known to cause CF disease.

<sup>‡</sup> The disease is very unlikely; however, if there are 2 CF mutations in trans, CF may be diagnosed.

<sup>§</sup> After a repeat sweat test, further evaluation depends on the results as implied above.

**Figure 16-1.** The CF diagnostic process for screened newborns. (From the National Institutes of Health. <http://www.ncbi.nlm.nih.gov/pubmed/18639722>. Accessed April 23, 2012.)

**Long-term management of CF patients** is best coordinated by experienced pediatric **pulmonary specialists** and includes minimizing airway reactivity and infections, optimizing nutritional status, and providing ongoing psychosocial support. The prognosis varies depending on disease severity. Infants with severe lung disease can die in early childhood, but most patients reach adolescence or adulthood. Mean survival for persons with CF now exceeds 35 years.

## COMPREHENSION QUESTIONS

- 16.1 A term infant delivered vaginally develops vomiting and abdominal distention after 10 hours of birth. No stool passage has been noted. An abdominal radiograph shows distended small bowel loops and a “bubbly” pattern in a portion of intestine; the colon is narrow. Which of the following should you tell the parents?
- A. You would like to consult a pediatric surgeon because you suspect that their child has Hirschsprung disease.
  - B. The child most likely has necrotizing enterocolitis, a condition more commonly seen in premature infants. Therefore, you question the child’s supposed gestational age.
  - C. You are concerned about the possibility of meconium ileus and would like to obtain some family history.
  - D. You believe that the child simply is constipated and would like to change to a soy-based formula to see whether the baby tolerates this better.
  - E. The child’s symptoms and radiograph findings most likely are normal.
- 16.2 Appropriate clinical management of the patient in Question 16.1 includes which of the following?
- A. Change from enteral to intravenous feeds; obtain genetics consultation for the next morning.

- B. Change from enteral to intravenous feeds, obtain a blood culture, and initiate antibiotics.
- C. Change from enteral to intravenous feeds, place a nasogastric tube, and obtain an emergency pediatric surgery consultation.
- D. Change from cow's milk to soy-based infant formula and continue to observe the infant.
- E. Do not change your current management.

16.3 A 10-year-old boy has a history of recurrent sinusitis and multiple episodes of pneumonia. A sweat electrolyte test result is within the normal range. Which of the following can be removed from your differential diagnosis now?

- A. Atopy
- B. Primary ciliary dyskinesia (Kartagener syndrome)
- C. Gastroesophageal reflux disease (GERD)
- D. Cystic fibrosis
- E. Severe combined immunodeficiency

16.4 A 2-month-old infant presents with 5 days of wheezing and diarrhea. Parents report a subjective fever. She continues to breastfeed well. Laboratory abnormalities that could suggest cystic fibrosis include all of the following except:

- A. Hyponatremia and hypochloremia
- B. Metabolic alkalosis
- C. Neutropenia
- D. Elevated prothrombin time (PT)
- E. Anemia with a reticulocyte count of 10%

## ANSWERS

16.1 C. Meconium ileus, inspissated meconium obstructing the distal ileum, is thought to be caused by deficiency of proteolytic enzymes. Obstruction begins *in utero*, resulting in underdevelopment of distal lumina. It is almost always associated with CF. Intestinal atresia and Hirschsprung



disease (congenital aganglionic megacolon) cause similar clinical pictures, but the radiographic findings for this child are most consistent with meconium ileus. Necrotizing enterocolitis also causes emesis and abdominal distension but occurs primarily in extremely low-birth-weight infants (ie, <1000 g); the colon would be expected to be of normal size. Constipation is not consistent with this baby's clinical picture or the described radiographic picture.

- 16.2 C. Meconium ileus is a surgical emergency, as volvulus and perforation with peritonitis are not uncommon complications.
- 16.3 E. Children with severe combined immunodeficiency will present in the first few months of life, and without stem cell transplant most die in the first year of life. CF cannot be ruled out since there can be false-negative test results; the sweat chloride test should be repeated and a full review of systems for other gastrointestinal or genitourinary symptoms should be done. Bronchiectasis and chronic sinusitis are characteristic of ciliary dyskinesia syndromes. Recurrent pneumonia and sinusitis can occur as complications of GERD and atopic disease.
- 16.4 C. Infants with CF will lose excess amounts of sodium chloride in their sweat resulting in a hyponatremic, hypochloremic metabolic alkalosis. Malabsorption of fats and protein are major causes of morbidity for patients with CF; these infants will need supplements of the fat-soluble vitamins (A, D, E, and K). Breastfed infants are already at risk for vitamin K deficiency, which manifests as an elevated PT. Elevated reticulocyte counts are seen with hemolysis (and acute bleeding) and would be seen with vitamin E deficiency. Neutropenia can occur with viral infections but is not a hallmark of CF.

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## CLINICAL PEARLS

- Cystic fibrosis (CF) involves a defect in mucus secretion and eccrine sweat gland function, resulting in various visceral lumina obstructions and excessive electrolyte secretion.
- Extrapulmonary signs and symptoms, such as digital clubbing, recurrent sinusitis, growth retardation, and fat malabsorption, are clues to the diagnosis of cystic fibrosis.
- A negative sweat chloride test result does not preclude cystic fibrosis.

- Meconium ileus in the newborn period is nearly pathognomonic for cystic fibrosis.
- 

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### CASE 17

A mother brings her previously healthy 6-year-old son to your clinic because he has been limping and complaining of left leg and knee pain for 1 week. He has experienced no recent trauma, and his past medical history is unremarkable. His physical examination reveals a temperature of 100°F (37.8°C) orally with no lower extremity swelling, misalignment, or weakness. He has tenderness over the right knee, hepatosplenomegaly, and petechiae on his cheeks and chest.

- What is the most likely diagnosis?
- What is the next step in the evaluation?

**ANSWERS TO CASE 17: Acute Lymphoblastic Leukemia**

*Summary:* A 6-year-old boy with a 1-week history of leg pain and limping. He has a low-grade fever, hepatosplenomegaly, and petechiae on his face and chest.

- **Most likely diagnosis:** Acute lymphoblastic leukemia (ALL).
- **Next step in the evaluation:** Complete blood count with platelets and differential.

## ANALYSIS

### *Objectives*

1. Describe the clinical manifestations of ALL.
2. Describe the laboratory and radiologic tests used in diagnosing ALL.
3. Know the treatment plan for a child with newly diagnosed ALL.
4. Understand the long-term survival and follow-up issues for children with ALL.

### *Considerations*

This patient has several manifestations of ALL, including leg and joint pain, fever, petechiae, and hepatosplenomegaly. Most of the signs and symptoms of ALL result from either replacement of normal bone marrow components with clonal proliferation of a single lymphoblast that has undergone malignant transformation, or from infiltrates of extramedullary sites by these malignant lymphoid cells. Rapid diagnosis and referral to a pediatric cancer center can increase survival.

APPROACH TO:

**Acute Lymphoblastic Leukemia**

## DEFINITIONS

**EXTRAMEDULLARY:** Areas of the body outside of the bone marrow.

**LYMPHOBLAST:** A large, primitive, undifferentiated precursor cell not normally seen in the peripheral circulation.

**GRANULOCYTOPENIA:** A reduction in total circulating leukocytes.

**PANCYTOPENIA:** A reduction in circulating erythrocytes, leukocytes, and platelets.

**THROMBOCYTOPENIA:** A reduction in circulating platelets.

## CLINICAL APPROACH

**Leukemia is the most common childhood cancer**, accounting for **approximately 40% of all pediatric malignancies**. **Acute lymphoblastic leukemia** affects the **lymphoid cell line** and comprises approximately 75% of leukemia cases in children. Acute myeloblastic leukemia (AML) affects the myeloid cell line (granulocytes, monocytes, and can affect erythrocytes or megakaryocytes) and comprises approximately 20% of childhood leukemia. The clinical manifestations of AML and ALL are similar. In the United States, childhood **ALL has a peak incidence at age 2 to 4 years** and occurs more frequently in **boys**. Children with certain chromosomal abnormalities, such as Down syndrome and Fanconi anemia, have an increased risk of ALL.

ALL is often called the “great imitator” because of its nonspecific symptoms, including anorexia, irritability, lethargy, pallor, bleeding, petechiae, leg and joint pain, and fever. A physical examination includes the child’s general appearance and energy level, vital signs (note if antipyretics taken), bleeding, bruising, petechiae, pallor, pain upon palpating bones or joints, and hepatosplenomegaly. Differential diagnoses include idiopathic thrombocytopenic purpura (ITP), aplastic anemia, mononucleosis, juvenile rheumatoid arthritis, and leukemoid reaction:

- Idiopathic thrombocytopenic purpura is a common cause of bruising and petechiae because of low platelet levels; however, anemia, leukocyte disturbances, and hepatosplenomegaly are absent.
- Aplastic anemia causes pancytopenia and fever; lymphadenopathy, arthralgias, bone pain, and hepatosplenomegaly are unusual findings.
- Children with infectious mononucleosis (ie, Epstein-Barr virus [EB virus]) or other acute viral illnesses may present with fever, malaise, adenopathy, splenomegaly, and lymphocytosis. Atypical lymphocytes

resembling leukemic lymphoblasts are characteristic of these viral illnesses.

- Leukemoid reactions may be observed in bacterial sepsis, pertussis, acute hemolysis, granulomatous disease, and vasculitis. The leukemoid reaction resolves as the underlying disease is treated.

Children with ALL who present with fever, arthralgias, arthritis, or a limp frequently are diagnosed initially with juvenile rheumatoid arthritis (JRA). Anemia, leukocytosis, and mild splenomegaly may also be seen in JRA, causing even more confusion. **A bone marrow examination may be required to differentiate ALL from other diagnoses.**

Infiltration of the marrow by other types of malignant cells (neuroblastoma, rhabdomyosarcoma, Ewing sarcoma, and retinoblastoma) occasionally produces pancytopenia. These tumor cells usually are found in clumps in the normal marrow but occasionally replace the marrow completely.

**Almost half of the children with newly diagnosed leukemia have total leukocyte counts less than  $10,000/\text{mm}^3$ .** Leukemic blasts may not be seen in the peripheral blood smear. Therefore, the diagnosis of leukemia is established by **examination of bone marrow**, most commonly aspirated from the posterior iliac crest.

**A normal marrow contains less than 5% blasts; a minimum of 25% blasts confirms the diagnosis.** Approximately two-thirds of children with ALL have leukemic cell karyotypic abnormalities, including changes in chromosome number (ie, hypodiploidy or hyperdiploidy) or chromosome structure (translocation, deletions, inversions).

A variety of markers can help gauge prognosis. In general, **girls have a better prognosis. African-American and Hispanic populations** historically have **lower remission and higher relapse rates**, although newer studies suggest this might be due to factors other than race. Children with ALL who are **younger than 1 year and those who are older than 10 years** of age have a **worse prognosis. Higher leukocyte counts**, especially if higher than  $50,000/\text{mm}^3$ , have an unfavorable prognosis. Patients with **T-cell immunophenotype** typically have a worse outcome than those with B-precursor ALL. The karyotypes of leukemic cells have diagnostic, prognostic,

and therapeutic significance. Patients with hyperdiploidy generally have a more favorable prognosis; those with hypodiploidy and pseudodiploidy do less well. Translocations with a poor outcome include t(9;22) (Philadelphia chromosome) in patients with pre-B ALL, and t(4;11) seen in infants with AML.

Workup includes a **lumbar puncture** to examine the central nervous system (CNS) for early leukemic involvement; a **higher number of blasts in the cerebro-spinal fluid is associated with a worse prognosis**. A **chest radiograph** is performed to detect a **mediastinal mass**. Bone radiographs may show altered medullary trabeculation, cortical defects, or transverse radiolucent lines; these radiologic findings lack prognostic significance and usually are unnecessary.

**Combination chemotherapy is the principal therapy.** The therapy involves several phases: remission induction, CNS therapy, consolidation and intensification, and maintenance. Induction therapy, a combination of prednisone, vincristine, and asparaginase, produces remission within 4 weeks in approximately 98% of children with non-high-risk ALL. Intrathecal therapy ( $\pm$  craniospinal irradiation) has decreased the incidence of CNS leukemia as a primary site of relapse from 50% to approximately 3% to 6%. Consolidation treatment, aimed at further reducing residual leukemia, delivers multiple chemotherapies in a relatively short period of time. Maintenance therapy with methotrexate and 6-mercaptopurine, vincristine, and prednisone is given for 2 to 3 years to prevent relapse; therapy is discontinued for children who remain in complete remission for 2 to 3 years.

**The 5-year survival rate for childhood ALL has steadily improved over the last 40 years and now is greater than 80%.** Late effects to be considered include neuropsychological deficits, seizures, and endocrine disturbances (ie, growth hormone deficiency) related to CNS prophylaxis; spermatogenesis dysfunction related to cyclophosphamide; delayed sexual maturation in boys who received irradiation of gonadal tissue due to leukemic invasion of the testes; leukoencephalopathy and neurodevelopmental problems (especially in post-CNS radiation patients); and secondary malignancies.

## COMPREHENSION QUESTIONS

- 17.1 A mother brings her 3-year-old son with Down syndrome to the clinic because his gums have been bleeding for 1 week. She reports that he has been less energetic than usual. Examination reveals that the child has an oral temperature of 100°F (37.8°C), pallor, splenomegaly, gingival bleeding, and bruises on the lower extremities. Which of the following is most likely?
- A. Aplastic anemia
  - B. Idiopathic thrombocytopenic purpura (ITP)
  - C. Leukemia
  - D. Leukemoid reaction
  - E. Megaloblastic anemia
- 17.2 A father brings to the clinic his 6-year-old son who currently is undergoing induction chemotherapy for ALL. The school will not allow the child to register until his immunizations are up-to-date. Which of the following is the best course of action?
- A. Call the school nurse or principal to inform him or her that this child should not receive immunizations while he is taking chemotherapy.
  - B. Update all immunizations except for measles-mumps-rubella (MMR) and varicella.
  - C. Update all immunizations except for oral polio vaccine.
  - D. Update all immunizations.
  - E. Call the school nurse or principal to inform him or her that this child will never receive immunizations because of the alteration in his immune system.
- 17.3 A mother brings to the clinic her 4-year-old son who began complaining of right knee pain 2 weeks ago, is limping slightly, is fatigued, and has had a fever to 100.4°F (38°C). Which of the following laboratory tests is most important?
- A. Antinuclear antibodies
  - B. Complete blood count (CBC) with differential and platelets
  - C. Epstein-Barr virus titer
  - D. Rheumatoid factor

E. Sedimentation rate

**17.4** Two weeks after a viral syndrome, a 2-year-old develops bruising and generalized petechiae that is more prominent over the legs. He has neither hepatosplenomegaly nor lymph node enlargement. Laboratory testing reveals a normal hemoglobin, hematocrit, and white blood cell count and differential. The platelet count is  $15,000/\text{mm}^3$ . Which of the following is the most likely diagnosis?

- A. Acute lymphoblastic leukemia
- B. Aplastic anemia
- C. Immune thrombocytopenic purpura
- D. Thrombotic thrombocytopenic purpura
- E. von Willebrand disease

## ANSWERS

**17.1 C.** A high susceptibility to leukemia is associated with certain heritable diseases (Klinefelter syndrome, Bloom syndrome, Fanconi syndrome, ataxia telangiectasia, neurofibromatosis) and chromosomal disorders such as Down syndrome. Children with Down syndrome have a 10- to 15-fold increased risk for developing leukemia. Siblings of an ALL patient have a two- to fourfold increased risk for ALL, and the monozygotic twin of a child who develops ALL in the first year of life has a >70% chance of also developing ALL. A few cases of ALL are associated with p53 gene aberrations. Overall, these genetic links account for a small number of total ALL cases.

**17.2 A.** Live virus vaccines are contraindicated for the child with ALL (and all members of the household) during chemotherapy and for at least 6 months after completion of treatment. Although the viruses in the vaccine are attenuated, immunosuppression from treatment can be profound and viral disease can result. Immunizations without live virus (diphtheria, tetanus, inactivated poliovirus vaccine, hepatitis A and B) are not absolutely contraindicated in this case, but the immunosuppression with chemotherapy often inhibits antibody responses.



- 17.3 **B.** This child has symptoms consistent with both JRA and leukemia. The CBC with differential and platelets is the best initial screening test. The leukocyte and platelet counts are normal to increased in JRA, and no blast cells are present. Frequently, blast cells are found on the peripheral smear with ALL. The child in the question ultimately may require a bone marrow aspiration.
- 17.4 **C.** Immune (or idiopathic) thrombocytopenic purpura (ITP) is common in children. In most cases, a preceding viral infection can be documented. The platelet count frequently is less than  $20,000/\text{mm}^3$ , but other laboratory test results are normal, including the bone marrow aspiration (which may show an increase in megakaryocytes). Treatment consists of observation or possibly intravenous immunoglobulin (IVIG), intravenous anti-D (in Rh-positive patients), immunosuppressives, or steroids. The history must be reviewed for other possible causes of thrombocytopenia, including recent MMR vaccination, drug ingestion, and human immunodeficiency virus.
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### CLINICAL PEARLS

- Leukemias are the most common childhood cancers, and acute lymphoblastic leukemia (ALL) represents approximately 75% of all leukemia cases in children.
  - Acute lymphoblastic leukemia has a peak incidence at the age of 2 to 4 years, and boys are affected more frequently.
  - Acute lymphoblastic leukemia is often called the “great imitator” because of its nonspecific symptoms of anorexia, irritability, lethargy, pallor, bleeding, petechiae, leg and joint pain, and fever.
  - Combination chemotherapy is the principal therapy for childhood acute lymphoblastic leukemia. Induction therapy produces remission within 4 weeks in approximately 98% of children with average-risk acute lymphoblastic leukemia.
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## CASE 18

You are called to the operating room to manage an infant recently born by emergency cesarean delivery. The mother, an 18-year-old with one previous child, received no prenatal care and arrived at the hospital approximately an hour prior to delivery. At delivery you find a large (4500 g), grayish-colored infant with poor tone, no spontaneous respirations, and a pulse of 100 beats per minute (bpm).

- What is the first step in the evaluation of this child?
- What is the most likely diagnosis?

► What is the next step in evaluation?

## ANSWERS TO CASE 18: **Infant of a Diabetic Mother**

*Summary:* A very large newborn with respiratory depression.

- **First step:** Resuscitation of the infant focuses on the **ABCs: A** (airway), **B** (breathing), and **C** (circulation). Oxygen is provided, and the infant is stimulated to breathe on his own. If these simple measures fail, bag-and-mask ventilation and endotracheal intubation may be required. Upon oxygenation, the infant's poor tone, color, and slow heart rate should resolve.
- **Most likely diagnosis:** Respiratory distress in an infant of a diabetic mother (IDM).
- **Next step:** Once the infant's cardiorespiratory status is stabilized, frequent checks for hypoglycemia over the next 24 hours are indicated.

## ANALYSIS

### *Objectives*

1. Recognize the clinical features of the IDM.
2. Know the management of the IDM.
3. Know the infant anomalies that are associated with pregestational diabetes.

### *Considerations*

**Fetal hyperinsulinism is a response to poorly controlled maternal hyperglycemia resulting in fetal macrosomia and increased fetal oxygen requirements.** These two factors can make the birth process difficult and result in neonatal distress.

**After delivery** and removal from the high-sugar *in utero* environment, the infant's hyperinsulinism can cause **hypoglycemia** and must be managed immediately to prevent further complications. A blood glucose level of 25 to 40 mg/dL requires immediate feeding. A level less than 25 mg/dL (or higher levels in symptomatic infants) is treated with intravenous glucose.

**Respiratory distress syndrome, polycythemia with hyperviscosity syndrome, hypocalcemia, hypomagnesemia, and hyperbilirubinemia** are other sequelae of gestational diabetes that may require management.

APPROACH TO:

**Infant of a Diabetic Mother**

## DEFINITIONS

**GESTATIONAL DIABETES:** Persistent hyperglycemia during pregnancy, with serum glucose levels greater than 95 mg/dL in the fasting state and above the thresholds for the oral glucose tolerance test.

**HYPOGLYCEMIA:** A blood glucose level less than 40 mg/dL is the usual definition, although other definitions exist. Symptoms include lethargy, listlessness, poor feeding, temperature instability, apnea, cyanosis, jitteriness, tremors, seizure activity, and respiratory distress.

**MACROSOMIA:** Larger than normal baby with the birth weight exceeding the 90th percentile for gestational age, or any birth weight >4 kg.

**POLYCYTHEMIA:** In a newborn, a central hematocrit >65. This can lead to thrombosis if the infant is symptomatic and remains untreated.

**CAUDAL REGRESSION SYNDROME:** Rare congenital malformation found almost exclusively in the IDM, characterized by hypoplasia of the sacrum and lower extremities.

## CLINICAL APPROACH

**Diabetes affects an average of 7% of pregnancies.** For most women, the condition is transient, occurring during pregnancy and disappearing after delivery. **Women are screened for gestational diabetes (GDM) between 24 and 28 weeks of pregnancy** (but can be screened earlier if considered high risk). It is classified according to maternal age when the condition is first diagnosed (onset during gestation, or pregestational), the duration of symptoms, and the presence of vasculopathy (the “White Classification”). Women who require insulin therapy are at higher risk for a poor perinatal outcome than those whose carbohydrate intolerance can be managed by diet

alone. Women with preexisting diabetes are followed closely; **many of the congenital malformations associated with gestational diabetes are thought to result from hyperglycemia early in the pregnancy.**

The fetal pancreas begins producing insulin during the fourth month of gestation and becomes functionally significant after week 26, when macrosomia due to maternal hyperglycemia may first be noted. Increased infant weight and length occur because of increased adipose tissue deposition and the growth hormone effects of insulin. Increased glycogen is stored in the infant liver, kidney, skeletal muscle, and heart. Height and head circumference are less significantly affected because insulin does not affect bone and brain growth. Thus, the weight of an IDM typically is in its shoulders and abdomen.

Macrosomia, increased oxygen requirements, and placental insufficiency can lead to perinatal asphyxia and increased production of erythropoietin. The resultant **polycythemia** contributes to elevated bilirubin levels and can cause hyperviscosity syndrome with resultant venous thromboses (kidney, sinus), stroke, necrotizing enterocolitis, or persistent pulmonary hypertension. **Hypocalcemia** is common and results in irritability, sweating, or seizures.

**Infants of a diabetic mother are at increased risk for congenital malformations, including congenital heart disease, neural tube defects, small left colon syndrome, and the caudal regression syndrome.** Their large size at birth can complicate vaginal delivery; shoulder dystocia is a common problem in the vaginal delivery of a large IDM. Conversely, an IDM may be small for gestational age if the mother's diabetes is associated with severe vascular disease and resultant placental insufficiency. IDMs may be small in infancy but are often overweight in childhood and adolescence.

## COMPREHENSION QUESTIONS

- 18.1 A 35-week-gestation infant is delivered via cesarean section because of macrosomia and fetal distress. The mother has class D pregestational diabetes (insulin-dependent, with vascular disease); her hemoglobin A1c is 20% (normal 8%). This infant is at risk for birth asphyxia, cardiac septal hypertrophy, polycythemia, and which of the following?
- A. Congenital dislocated hip
  - B. Dacryostenosis

- C. Hyaline membrane disease
- D. Hyperglycemia
- E. Pneumothorax

18.2 A term infant weighing 4530 g is born without complication to a mother with class A pregestational diabetes (non-insulin requiring). His initial glucose level is 30 mg/dL, but the level after he consumes 30 cc of infant formula is 50 mg/dL, and another level obtained 30 minutes later is 55 mg/dL. His physical examination is unremarkable except for his large size. Approximately 48 hours later, he appears mildly jaundiced. Vital signs are stable, and he is eating well. Which of the following serum laboratory tests are most likely to help you evaluate this infant's jaundice?

- A. Total protein, serum albumin, and liver transaminases
- B. Total and direct bilirubin, liver transaminases, and a hepatitis panel
- C. Total bilirubin and a hematocrit
- D. Total bilirubin and a complete blood count
- E. Total and direct bilirubin and a complete blood count with differential and platelets

18.3 A premature infant of a class B pregestational (insulin-requiring, but without vascular disease) diabetic mother is delivered via cesarean section due to fetal distress. The mother's axillary temperature at delivery is 98.6°F (37°C). The child has poor color and tone, no spontaneous cry, minimal respiratory effort, and a weak pulse of 80 bpm. After endotracheal intubation, the color and tone improve a bit, but she still has perioral cyanosis and her heart rate is 90 bpm. Which of the following is the most likely cause of her persistent distress?

- A. Hypocalcemia
- B. Hypoglycemia
- C. Impaired cardiac function
- D. Renal failure
- E. Sepsis

- 18.4 A term girl born to a mother with class C pregestational diabetes (insulin-dependent, but without vascular disease) requires endotracheal intubation at delivery for poor respiratory effort, tone, and color. Her initial serum glucose level is 10 mg/dL, and the level stabilizes over 36 hours with intravenous administration of glucose. She is extubated and begins to breastfeed. On the third day of life, she has been feeding every 3 hours and voided twice; physical examination is remarkable for macrosomia, plethora, and a new abdominal mass. Which of the following is the most likely cause of the abdominal mass?
- A. Hydronephrosis
  - B. Infarction of the spleen
  - C. Small left colon syndrome
  - D. Liver engorgement
  - E. Renal vein thrombosis

## ANSWERS

- 18.1 C. Infants born to mothers with poorly controlled diabetes are at risk for respiratory distress syndrome (surfactant deficiency) at later gestational ages than seen in infants born to mothers who do not have diabetes.
- 18.2 C. This baby most likely has hyperbilirubinemia secondary to liver immaturity, possibly complicated by polycythemia. He should have a high level of unconjugated bilirubin and, in the absence of intrahepatic disease, a normal conjugated (or direct) portion. While choices D and E include the correct answer, additional tests are unnecessary for this otherwise healthy-appearing infant who continues to feed well. Therefore, C is the best answer to the question.
- 18.3 C. Infants born to mothers with poorly controlled gestational diabetes are at risk for congenital heart anomalies, hypertrophic cardiomyopathy, septal hypertrophy, conotruncal anomalies, and subaortic stenosis. This child's symptoms and the maternal diabetes history indicate a risk for cardiac problems. Sepsis can cause similar symptoms, but no risk factors for infectious disease are noted. This child is at risk for hypoglycemia, but hypoglycemia alone would less likely explain all of her symptoms.

18.4 E. Renal vein thrombosis can present as an abdominal mass because the kidney becomes congested and palpable. The other classic components of its presentation, gross hematuria and thrombocytopenia, are seen in 25% of patients. Many patients will be oliguric. Hypertension is uncommon following an acute thrombosis but may occur as a late complication. Hydronephrosis is a common cause of abdominal or flank masses in neonates but is not the most likely given this infant's accompanying history. Small left colon syndrome presents with failure to pass meconium in the first 2 days of life with resultant abdominal distention and vomiting.

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### CLINICAL PEARLS

- Infants of diabetic mothers are at risk for perinatal complications, including hypoglycemia, hyperbilirubinemia, birth trauma, and congenital malformations.
  - Infants of diabetic mothers usually are heavier and longer than expected, but head circumference usually is normal. Infants of diabetic mothers can be small for gestational age if placental insufficiency is present.
  - Routine prenatal care includes screening for gestational diabetes.
- 

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## CASE 19

A mother is concerned that her 12-day-old son's face and chest are turning yellow. This infant was delivered vaginally after an uncomplicated term pregnancy. The baby had slight jaundice after the first day of life, but this resolved by the third day only to begin to return. The family history is significant for the father's mildly elevated bilirubin level, which was noted on a routine checkup. With the exception of jaundice, his physical examination is normal. He is formula feeding well and shows no signs of illness.

- ▶ What is the most likely diagnosis?
- ▶ What is the next step in evaluating this patient?

### ANSWERS TO CASE 19: **Gilbert Syndrome**

*Summary:* A healthy, 12-day-old, formula-fed male has jaundice.

- **Most likely diagnosis:** Gilbert syndrome.
- **Next step:** Serum bilirubin level.

## ANALYSIS

### *Objectives*

1. Understand the etiology of physiologic neonatal jaundice.
2. Identify the causes of pathologic jaundice in a newborn.
3. Know the treatment for neonatal jaundice.

### ***Considerations***

Neonatal hyperbilirubinemia results from higher rates of bilirubin production and a limited ability to excrete it. It includes physiologic jaundice and nonphysiologic jaundice. Gilbert syndrome, an example of a nonphysiologic cause of jaundice, is a genetic disorder of bilirubin metabolism, involving a decrease in the activity level of uridine diphosphate (UDP)-glucuronosyltransferase 1A1. Gilbert syndrome is a benign condition that does not require treatment; it has a prevalence rate of 2% to 10%. **This infant's father has a mildly elevated bilirubin that was incidentally discovered; he likely has Gilbert syndrome.** Risk factors for neonatal **physiologic** jaundice include maternal diabetes, cephalohematoma, male gender, Asian origin, prematurity, polycythemia, trisomy 21, cutaneous bruising, delayed bowel movement, upper gastrointestinal obstruction, hypothyroidism, swallowed maternal blood, and a sibling with physiologic jaundice. A variety of pathologic conditions can cause nonphysiologic jaundice when excessive unconjugated bilirubin accumulates:

- Red blood cells (RBCs) are lysed at too rapid a rate.
- Transmission of unconjugated bilirubin to the liver is interrupted.
- Liver enzyme deficiencies preclude appropriate metabolism of the unconjugated material.

Neonatal jaundice may present at birth or appear at any time during the neonatal period. Untreated severe unconjugated hyperbilirubinemia is potentially neurotoxic. Conjugated hyperbilirubinemia, although not neurotoxic, often signifies a serious underlying illness.

APPROACH TO:

**Neonatal Jaundice**

## **DEFINITIONS**

**CONJUGATED (DIRECT) BILIRUBIN:** Bilirubin chemically attached to a glucuronide by an enzymatic process in the liver.

**ERYTHROBLASTOSIS FETALIS:** Increased RBC destruction because of transplacental maternal antibody passage active against the infant's RBC antigens.

**HEMOLYSIS:** Rapid breakdown of RBCs. Clinical and laboratory findings might include a rapid rise of serum bilirubin level ( $>0.5$  mg/dL/h), anemia, pallor, reticulocytosis, and hepatosplenomegaly.

**GILBERT SYNDROME:** A genetic disorder of bilirubin metabolism, involving a decrease in the activity level of UDP-glucuronosyltransferase 1A1.

**KERNICTERUS:** A neurologic syndrome resulting from unconjugated bilirubin deposition in brain cells, especially the basal ganglia, globus pallidus, putamen, and caudate nuclei. Less mature or sick infants have greater susceptibility. Lethargy, poor feeding, and loss of Moro reflex are common initial signs.

**POLYCYTHEMIA:** A central hematocrit of 65% or higher, which can lead to blood hyperviscosity.

**UNCONJUGATED (INDIRECT) BILIRUBIN:** Bilirubin yet to be enzymatically attached to a glucuronide in the liver.

## CLINICAL APPROACH

**Physiologic jaundice comprises primarily unconjugated hyperbilirubinemia observed during the first week of life in approximately 60% of full-term infants and 80% of preterm infants.** Physiologic jaundice is established by precluding known jaundice causes through history, clinical, and laboratory findings. Newborn infants have a limited ability to conjugate bilirubin and cannot readily excrete unconjugated bili-rubin. Jaundice usually begins on the face and then progresses to the chest, abdomen, and feet. **Full-term newborns usually have peak bilirubin concentrations of 5 to 6 mg/dL between the second and fourth days of life.**

**Findings suggestive of nonphysiologic jaundice** include: (1) appearance in the first 24 to 36 hours of life; (2) bilirubin rate of rise greater than 5

mg/dL/24 h; (3) bilirubin greater than 12 mg/dL in a full-term infant without other physiologic jaundice risk factors listed; and (4) jaundice that persists after 10 to 14 days of life. Nonphysiologic etiologies are commonly diagnosed in a jaundiced infant who has a family history of hemolytic disease or in an infant with concomitant pallor, hepatomegaly, splenomegaly, failure of phototherapy to lower bilirubin, vomiting, lethargy, poor feeding, excessive weight loss, apnea, or bradycardia. **Causes of nonphysiologic jaundice include septicemia, biliary atresia, hepatitis, galactosemia, hypothyroidism, cystic fibrosis, congenital hemolytic anemia** (eg, spherocytosis, maternal Rh or blood type sensitization), or **drug-induced hemolytic anemia**.

**Jaundice presenting within the first 24 hours of life requires immediate attention;** causes include **erythroblastosis fetalis, hemorrhage, sepsis, cytomegalic inclusion disease, rubella, and congenital toxoplasmosis**. Unconjugated hyper-bilirubinemia can cause **kernicterus**, the signs of which mimic sepsis, asphyxia, hypoglycemia, and intracranial hemorrhage. Lethargy and poor feeding are common initial signs, followed by a gravely ill appearance with respiratory distress and diminished tendon reflexes.

**Approximately 2% of breast-fed full-term infants develop significant unconjugated bilirubin elevations (breast-milk jaundice) after the seventh day of life; concentrations up to 30 mg/dL** during the second to third week can be seen. If breast-feeding is continued, the levels gradually decrease. Formula substitution for breast milk for 12 to 24 hours results in a rapid bilirubin level decrease; breastfeeding can be resumed without return of hyperbilirubinemia.

Infants with Gilbert syndrome may appear to have a prolonged physiologic neonatal jaundice. After the newborn period, patients will have a mildly elevated indirect bilirubin (<5 mg/dL) and are more likely to exhibit jaundice after fasting.

Full-term, asymptomatic, low-risk but jaundiced infants are monitored with serum bilirubin levels. Significant hyperbilirubinemia requires a diagnostic evaluation, including measurement of indirect and direct bilirubin concentrations, hemoglobin level, reticulocyte count, blood type, Coombs test (indirect Coombs measures antibodies to RBCs in the blood; direct Coombs test identifies antibodies on surface of the infant's RBCs), and peripheral

blood smear examination. Estimates of serum bilirubin concentrations that are based solely on clinical examination are not reliable. **Noninvasive, transcutaneous measurement** using multiwavelength spectral reflectance is an alternative to serum measurement.

**Phototherapy** is often used to treat unconjugated hyperbilirubinemia, with the unclothed infant placed under a bank of lights, the eyes shielded, and hydration maintained. The light changes the skin's bilirubin isomerization into an excretable form. For full-term infants without hemolysis, **phototherapy** is initiated at the following bilirubin levels: 16-18 mg/dL at an age of 24 to 48 hours; 16-18 mg/dL at 49 to 72 hours; and more than or equal to 20 mg/dL at 72 hours or more.

**Exchange transfusion** is needed in a small number of jaundiced infants who do not respond to conservative measures. Small aliquots of the infant's blood are removed via a blood vessel catheter and replaced with similar aliquots of donor blood. Risks of this procedure include air embolus, volume imbalance, arrhythmias, acidosis, respiratory distress, electrolyte imbalance, anemia or polycythemia, blood pressure fluctuation, infection, and necrotizing enterocolitis.

## COMPREHENSION QUESTIONS

- 19.1 Which of the following decreases the risk of neurologic damage in a jaundiced newborn?
- A. Acidosis
  - B. Displacement of bilirubin from binding sites by drugs such as sulfisoxazole
  - C. Hypoalbuminemia
  - D. Sepsis
  - E. Maternal ingestion of phenobarbital during pregnancy
- 19.2 You are to return a telephone call to the mother of an 8-day-old infant who continues to have jaundice that was first noted on the second day of life. The latest data show that his most recent total and direct bilirubin levels are 12.5 and 0.9 mg/dL, respectively. You look over your chart and see that he and his mother have O type blood, the direct and indirect Coombs test is negative, his reticulocyte count is 15%, and a smear of

his blood reveals no abnormal cell shapes. He is bottle-feeding well, produces normal stools and urine, and has gained weight well. Which of the following diagnoses remains in your differential diagnosis?

- A. Gilbert syndrome
- B. Disseminated intravascular coagulation (DIC)
- C. Spherocytosis
- D. Polycythemia
- E. An undiagnosed blood group isoimmunization

19.3 The hyperbilirubinemia associated with Crigler-Najjar syndrome type I is caused by which of the following?

- A. Increased production of bilirubin
- B. Impaired conjugation of bilirubin
- C. Deficient hepatic uptake of bilirubin
- D. Severe deficiency of uridine diphosphate-glucuronosyltransferase
- E. Glucose-6-phosphate dehydrogenase deficiency

19.4 A 30-hour-old full-term infant has face and chest jaundice. He is breastfeeding well and has an otherwise normal examination. His bilirubin level is 15.5 mg/dL. Which of the following is the most appropriate course of action?

- A. Recommend cessation of breast-feeding for 48 hours and supplement with formula.
- B. Start phototherapy.
- C. Wait 6 hours and retest the serum bilirubin level.
- D. Start an exchange transfusion.
- E. No action is needed.

## ANSWERS

19.1 E. Administration of phenobarbital induces glucuronyl transferase, thus reducing neonatal jaundice. Sepsis and acidosis increase the risk of neurologic damage by increasing the blood-brain barrier's permeability

to bilirubin. Hypoalbuminemia reduces the infant's ability to transport unconjugated bilirubin to the liver, and similarly drugs that displace bilirubin from albumin elevate free levels of unconjugated bilirubin in the serum.

- 19.2 **A.** Gilbert syndrome would present with a negative Coombs test, a normal (or low) hemoglobin, a normal (or slightly elevated) reticulocyte count, and prolonged hyperbilirubinemia. Red cell morphology would be abnormal in DIC and spherocytosis, polycythemia would present with an elevated hemoglobin level (that listed above is normal for a newborn), and blood group isoimmunization would present with a positive Coombs test.
- 19.3 **D.** Although all infants are relatively deficient in uridine diphosphate-glucuronosyltransferase, those with Crigler-Najjar syndrome type I have a severe deficiency, causing high bilirubin levels and encephalopathy. Treatment is phototherapy. Encephalopathy is rare with Crigler-Najjar syndrome type II, in which bilirubin levels rarely exceed 20 mg/dL.
- 19.4 **B.** Although the etiology of the hyperbilirubinemia must be investigated, phototherapy should be started.
- 

## CLINICAL PEARLS

- Physiologic jaundice, observed during the first week of life in the majority of infants, results from higher bilirubin production rates and a limited ability of excretion. The diagnosis is established by precluding known causes of jaundice based on history and clinical and laboratory findings.
  - Nonphysiologic jaundice is caused by septicemia, biliary atresia, hepatitis, galactosemia, hypothyroidism, cystic fibrosis, congenital hemolytic anemia, drug-induced hemolytic anemia, or antibodies directed at the fetal RBC.
  - High levels of unconjugated bilirubin may lead to kernicterus, an irreversible neurologic syndrome resulting from brain cell bilirubin deposition, especially in the basal ganglia, globus pallidus, putamen, and caudate nuclei. Less mature or sick infants are at greater risk. The signs and symptoms of kernicterus may be subtle and similar to those of sepsis, asphyxia, hypoglycemia, and intracranial hemorrhage.
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### CASE 20

A 10-year-old boy in respiratory distress arrives late in the evening to the emergency department (ED); he has a 2-hour history of rapid breathing and a complaint that his chest hurts. His mother gave him two nebulizer treatments without improvement. She tells you that this is the fourth time in 3 months that he has required ED visits for similar symptoms. Your initial examination reveals an afebrile male with a respiratory rate of 60 breaths per minute and a heart rate of 120 beats/min (bpm). You note that his pulse varies in amplitude with respiration. His blood pressure is normal, but his capillary refill is somewhat sluggish at 4 to 6 seconds. He is pale, appears drowsy, has mild perioral cyanosis, and is using accessory chest muscles to breathe. You hear only faint wheezing on chest auscultation.

- What are the initial steps in evaluating this patient?



- ▶ What is the most likely diagnosis?
- ▶ What is the next step in evaluation?

## ANSWERS TO CASE 20: Asthma Exacerbation

*Summary:* A 10-year-old boy with a multiple episodes of respiratory difficulty presents with tachypnea, perioral cyanosis, pulsus paradoxus, use of accessory muscles of breathing, slight wheezing, delayed capillary refill, and drowsiness.

- **Initial steps:** Treating this patient's respiratory distress is of immediate concern. The airway is evaluated first, followed by an evaluation of breathing, and finally assessment of the circulatory status (the "ABCs"). Initial management includes administration of oxygen, an inhaled  $\beta$ -agonist, and a systemic dose of prednisone. Intravenous administration of fluids and medications is indicated for a patient with this degree of distress. A stat blood gas determination and monitoring oxygen saturation levels will aid further management.
- **Most likely diagnosis:** Asthma exacerbation.
- **Next step in evaluation:** After initial stabilization, past medical and family histories (medications, triggers, frequency and severity of previous episodes, previous hospitalization or intensive care unit admissions) and a review of systems are obtained. The physical examination, blood gas report, and response to initial treatments will determine subsequent management.

## ANALYSIS

### *Objectives*

1. Know the acute management of asthma exacerbation.
2. Know how to classify the severity of an asthma exacerbation.
3. Know the approach to long-term management of asthma and prevention of exacerbations.

### *Considerations*

This child's history of ED visits for respiratory difficulty and his presenting symptoms point to asthma as the most likely diagnosis; less likely conditions include cystic fibrosis, foreign-body aspiration, and congestive heart failure. The National Institutes of Health, National Heart, Lung, and Blood Institute (NHLBI) asthma guidelines suggest this child's exacerbation is severe and requires immediate, intensive treatment. **His drowsiness is of particular concern, indicating impending respiratory failure;** his respiratory and circulatory status must be assessed frequently. The **paucity of wheezes** results from **severe airway obstruction** and reduced air movement; **wheezing is likely to increase as therapy allows more air movement.**

APPROACH TO:

**Asthma Exacerbation**

## DEFINITIONS

**ASTHMA:** The diagnosis when: (1) episodic symptoms of airflow obstruction are present; (2) airflow obstruction is at least partially reversible; and (3) alternative diagnoses are excluded.

**ASTHMA EXACERBATION:** Characterized by the triad of bronchoconstriction, airway inflammation, and mucus plugging.

**PULSUS PARADOXUS:** A blood pressure that varies more widely with respiration than normal. A variance of greater than 10 mm Hg between inspiration and expiration suggests obstructive airway disease, pericardial tamponade, or constrictive pericarditis.

**SPIROMETRY:** A test of pulmonary function. For patients with asthma, this test demonstrates airflow obstruction and reversibility, and can be used to determine an individual's response to treatment.

## CLINICAL APPROACH

Asthma accounts for approximately three million visits to pediatricians per year in the United States. The **median age at onset is 4 years**, but 20% of children develop symptoms within the first year of life. **Atopy and a family history** of asthma are strong risk factors for its development, as is respiratory

infection early in life; between 40% and 50% of children with **respiratory syncytial virus (RSV) bronchiolitis** later develop asthma. More than half of children with asthma have symptom resolution by young adulthood, but many have abnormal pulmonary function tests only to become symptomatic in later adulthood. Heavy exposure to pollution, allergens, or cigarette smoke makes resolution less likely. A chronic nighttime cough might be a harbinger of asthma.

**Airway inflammation in asthma is a result of mast cell activation.** An immediate immunoglobulin (Ig) E response to environmental triggers occurs within 15 to 30 minutes and includes vasodilation, increased vascular permeability, smooth-muscle constriction, and mucus secretion. Common triggers include dust mites, animal dander, cigarette smoke, pollution, weather changes, upper respiratory infections, certain drugs (ie,  $\beta$ -adrenergic antagonists, and some nonsteroidal anti-inflammatory agents), and exercise (particularly when performed in a cold environment). Two to four hours after this acute response, a **late-phase reaction (LPR)** begins. The LPR is **characterized by infiltration of inflammatory cells into the airway parenchyma**; it is responsible for the chronic inflammation seen in asthma. Airway hyperresponsiveness may persist for weeks after the LPR.

Asthma management involves classifying the disease severity and identifying and minimizing exposure to triggers. Severity is defined as either intermittent or persistent; persistent asthma is further divided into mild, moderate, or severe. Allergy testing can be helpful in some situations. Pharmacotherapy for the child's asthma symptoms follows NHLBI guidelines (available at <http://www.nhlbi.nih.gov/guide-lines/asthma/asthsumm.pdf>). Adequate long-term management depends on reinforcement with the patient and family of the goals of therapy. Repeat objective assessment of lung function is achieved with spirometry performed in the clinic and peak expiratory flow measurements obtained at home.

**Pharmacotherapy** for asthma includes  **$\beta$ -adrenergic agonists, anticholinergics, anti-inflammatory agents, and leukotriene modifiers**. The NHLBI guidelines provide a stepwise approach to administration of these medications.

**$\beta$ -Adrenergic agonists (ie, albuterol) rapidly reverse bronchoconstriction via  $\beta_2$ -receptors on bronchial smooth muscle cells; they do not significantly inhibit the LPR.** These agents also can be used

immediately prior to exercise or exposure to allergens to minimize the acute asthmatic response. Toxicity includes tachycardia and muscle tremor. Increased levels of drug are delivered to the lungs and toxicity is decreased when these medications are delivered through inhalation routes (nebulizer or inhaler) as compared to the oral route. When inhalers are used, a reservoir device (“spacer”) is used to maximize drug delivered to the lungs. Patients must not over-rely on short-acting inhalers because this practice is associated with death in severe asthma attacks.

**Anticholinergics** may be useful in the **acute management** of asthma exacerbation but are of **little value in chronic therapy**; they work by inhibiting the vagal reflex at smooth muscles.

**Cromolyn and nedocromil**, anti-inflammatory drugs that act by reducing the immune response to allergen exposure, **become effective after 2 to 4 weeks of therapy**; they are successful in only 75% of patients. **Leukotriene modifiers** are safe and effective anti-inflammatory medications for long-term control for some patients. The **most potent available anti-inflammatory drugs are corticosteroids**, which are useful for acute exacerbations (oral or intravenous prednisone, prednisolone) and for chronic therapy (inhaled corticosteroids).

## COMPREHENSION QUESTIONS

- 20.1 A 12-year-old asthmatic girl presents to the ED with tachypnea, intracostal retractions, perioral cyanosis, and minimal wheezing. You administer oxygen, inhaled albuterol, and intravenous prednisone. Upon reassessment, wheezing increases in all fields, and the child’s color has improved. Which of the following is the appropriate explanation for these findings?
- A. The girl is not having an asthma attack.
  - B. The girl is not responding to the albuterol, and her symptoms are worsening.
  - C. The girl is responding to the albuterol, and her symptoms are improving.
  - D. The girl did not receive enough albuterol.

E. The albuterol was inadvertently left out of the inhalation treatment, and the girl received only saline.

20.2 A previously healthy 2-year-old girl presents with the complaint of acute-onset wheezing. Her mother denies previous wheezing episodes and denies a family history of asthma or atopy. The mother says that she left the child playing in her older brother's room. Approximately 20 minutes later she heard the child coughing and wheezing. Which of the following is the best next step in management?

A. Determining what the girl was playing with and ordering a chest radiograph

B. Referring the child to a pulmonologist

C. Prescribing antibiotics for a likely pneumonia

D. Administering an injection of intramuscular prednisone and sending her home

E. Accusing the mother of poor supervision of her child's health, because this obviously is not the first time the child has experienced these symptoms

20.3 A well-developed 4-month-old boy presents to the ED on a cold winter's night with the complaint of worsening respiratory distress and decreased oral intake. His parents report that he was well until yesterday, when he developed upper respiratory symptoms and a low-grade fever. Upon examination of the child, you note pallor and perioral cyanosis, a respiratory rate of 65 breaths/min, and tight wheezes throughout the chest. An arterial blood gas shows a pH of 7.15, a  $\text{PCO}_2$  of 65 mm Hg, and a serum bicarbonate of 20 mmol/L. Which of the following is the most likely explanation regarding the child's condition?

A. The child most likely has bronchiolitis and is at risk of respiratory failure.

B. The child most likely has bronchiolitis, and his symptoms should resolve in the emergency department with additional albuterol treatments.

C. The child should undergo upper endoscopy, as you suspect a tracheoesophageal fistula.

D. The child most likely has gastroesophageal reflux and has aspirated.

E. The child has a metabolic acidosis that is most likely due to bacterial sepsis.

20.4 A 15-year-old adolescent male uses his albuterol inhaler shortly after he mows the lawn because of a mild feeling of chest “tightness.” He later returns home early from dinner at a friend’s house when he has the sudden onset of wheezing, cough, and chest pain. Which of the following is the most likely explanation for these circumstances?

A. He likely aspirated a piece of grass.

B. His albuterol inhaler must be empty.

C. His albuterol inhaler must be outdated.

D. He is having a late-phase reaction.

E. He has been exposed to a new allergen that is more irritating than grass.

## ANSWERS

20.1 C. This child presented in severe respiratory distress. Her improved color indicates reversible symptoms, confirming the diagnosis of asthma. Increased wheezing is auscultated after albuterol treatment because lung areas previously obstructed are now opening, allowing additional airflow. Less-experienced examiners may misinterpret lack of air movement as “clear” breath sounds, further delaying appropriate medical management.

20.2 A. Young children, generally between 4 months and 3 years of age, normally put objects in their mouth, and they are prone to developing foreign-body aspirations. A pulmonologist ultimately may be needed to retrieve the object, but this would not be a first step.

20.3 A. The differential diagnosis for a wheezing baby is extensive. However, the sudden onset of respiratory symptoms in a previously healthy infant, particularly in association with fever, is most consistent with the diagnosis of bronchiolitis. Initial treatment for this baby includes oxygen and a trial of nebulized albuterol or epinephrine. A blood gas measurement should be obtained immediately for any patient who presents in severe respiratory distress. This child’s blood gas indices

show a marked respiratory acidosis. He will likely require mechanical ventilation and monitoring in an intensive care setting until his symptoms improve. Infants with wheezing caused by bronchiolitis do not always respond to  $\beta$ -agonists. Chest radiographs in infants with bronchiolitis typically show hyperinflated lungs with areas of atelectasis. Respiratory syncytial virus (RSV) and influenza A are common causes of bronchiolitis in infants in the wintertime, but several other viral causes are also possible. A careful history should be obtained to rule out less common causes of wheezing in an infant, such as recurrent aspiration or a congenital anomaly.

**20.4 D.** A late-phase reaction typically occurs 2 to 4 hours after an initial wheezing episode. It is caused by accumulation of inflammatory cells in the airway.

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### CLINICAL PEARLS

- The prevalence of asthma in Western countries has been increasing steadily, making this the most frequent admission diagnosis for children in many urban hospitals.
  - Atopy and a family history of asthma are risk factors for development of asthma; exposure to pollutants including cigarette smoke makes resolution less likely.
  - The late-phase reaction begins 2 to 4 hours after allergen exposure and is responsible for the chronic inflammation seen in asthma.
  - Acute and long-term management of asthma is guided by recommendations published by the National Heart, Lung, and Blood Institute.
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## CASE 21

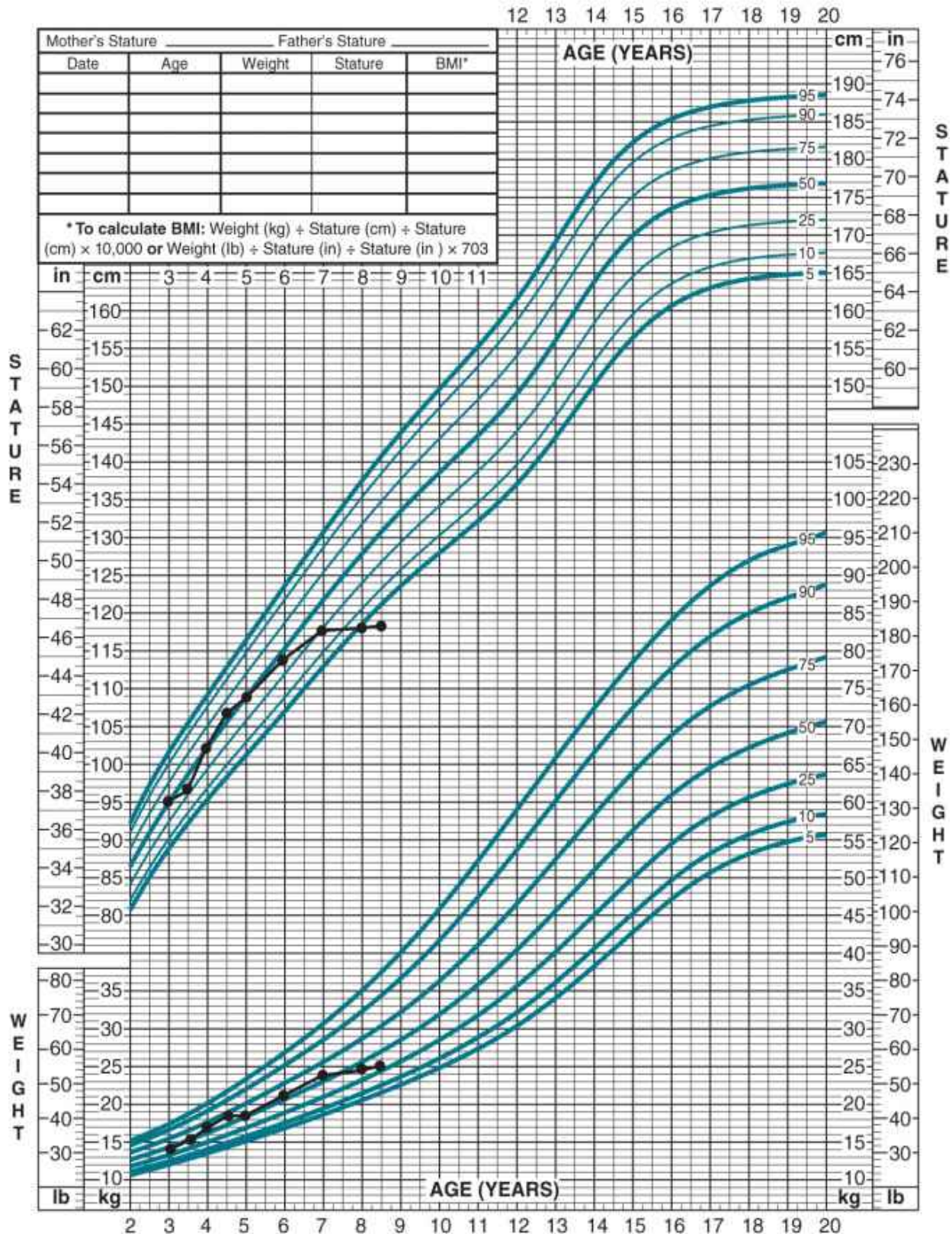
The parents of a healthy 8-year-old boy are concerned that he is the shortest child in his class. His height and weight growth curves are shown in [Figure 21-1](#) (see next page). He was a full-term infant, has experienced no significant medical problems, and is developmentally appropriate. Other than being small, his examination is normal. His upper and lower body segment measurements demonstrate normal body proportions. His father is 6 ft 4 in tall; he began pubertal development at 13 years of age. His mother is 5 ft 11 in tall; she had her first menstrual cycle at the age of 14 years.



**2 to 20 years: Boys**  
**Stature-for-age and Weight-for-age percentiles**

NAME \_\_\_\_\_

RECORD # \_\_\_\_\_



**Figure 21-1.** Childhood growth curve. (Reproduced from the Centers for Disease Control and Prevention.) Available at [http://www.cdc.gov/growthcharts/clinical\\_charts.htm](http://www.cdc.gov/growthcharts/clinical_charts.htm). Accessed on April 19, 2012.

- ▶ What is the most likely diagnosis?
- ▶ What is the best diagnostic test?
- ▶ What is the best therapy?

### ANSWERS TO CASE 21: **Growth Hormone Deficiency**

*Summary:* An 8-year-old boy with no significant medical history and a normal examination presents with failure to grow.

- **Most likely diagnosis:** Growth hormone (GH) deficiency.
- **Best diagnostic test:** Screening tests might include a complete blood count (CBC) and erythrocyte sedimentation rate (ESR); electrolytes and general health chemistry panel; urinalysis; serum for thyroid function studies, insulin-like growth factor-1 (IGF-1), and insulin-like growth factor-binding protein-3 (IGF-BP3); bone age radiograph; and, if this were a girl, possibly chromosomal karyotype.
- **Best therapy:** Replace GH via injection.

## ANALYSIS

### *Objectives*

1. Understand the common causes of growth delay in children.
2. Appreciate the evaluation strategies for the various forms of growth failure.
3. Learn treatment options for common causes of childhood growth delay.

### *Considerations*

This patient has essentially stopped growing (or is growing at a rate less than expected). He has no medical problems and a normal examination. His

parents are tall, and their pubertal development was not delayed. An evaluation to determine the reason for his growth failure is appropriate.

## APPROACH TO:

### **Growth Hormone Deficiency**

## DEFINITIONS

**BONE AGE:** Childhood bone development occurs in a predictable sequence. Left wrist radiographs on children older than 2 years (or the knee in those younger) are compared to “normals” to determine how old the bones appear compared to chronologic age, thus providing an estimate of the remaining growth potential of the bones.

**CONSTITUTIONAL GROWTH DELAY:** A condition in which a healthy child’s growth is slower than expected but for whom one or more parents demonstrated a pubertal development delay and ultimately normal adult height. In this case, the “bone age” equals the “height age.”

**FAMILIAL SHORT STATURE:** A condition in which a short child is born to short parents who had normal timing of their pubertal development.

**HEIGHT AGE:** The age at which a child’s measured height is at the 50th percentile.

**IDIOPATHIC SHORT STATURE:** A condition in which a short stature diagnosis cannot be reached.

## CLINICAL APPROACH

Many parents become concerned if their child is noticeably shorter than their child’s peers. Many conditions can result in short stature; a growth and social history (to identify psychosocial growth failure), physical examination, and selected screening tests usually help to identify the problem’s etiology.

**In the first year of life, children grow at a rate of approximately 23 to 28 cm per year. This rate drops to approximately 7.5 to 13 cm per year for children aged 1 to 3 years. Until puberty, they grow approximately 4.5 to 7 cm per year. At puberty, growth increases to 8 to 9 cm per year for girls**

**and to 10 to 11 cm per year for boys.** By approximately 24 months of age, most children settle into a percentile growth channel, remaining there for the remainder of their childhood. Significant deviations from these expectations alert the clinician to potential growth problems (ie, “fall off their curve”).

**Constitutional growth delay is a common cause of short stature.** These children have no history or examination abnormalities. In contrast to children with GH deficiency, children with constitutional delay have a **growth rate that is normal**. Their family history is positive, however, for one or more parents with pubertal development delays (“late bloomers”) who developed normal adult height. A short child in a family with a classic history of “late bloomers” often requires no laboratory or radiographic evaluation. Sometimes a bone age is helpful to reassure the patient and family that much bone growth remains and normal height will be achieved. For some of these children, testosterone injections will hasten pubertal changes (which eventually will begin on their own without treatment); consultation with a pediatric endocrinologist can be helpful.

The child born to short parents often is short (**familial short stature**). The growth curve shows growth parallel to a growth line at or just below the third to fifth percentile. Laboratory and radiographic testing usually are not necessary; a **bone age equals the chronologic age**, indicating no “extra” growth potential. An estimate of a child’s ultimate height potential is calculated using the parents’ heights. A boy’s final height can be predicted as follows:  $(\text{Father's height in cm} + [\text{Mother's height in cm} + 13])/2$ . A girl’s final height can be predicted as follows:  $(\text{Mother's height in cm} + [\text{Father's height in cm} + 13])/2$ . Reassurance is indicated for children with familial short stature.

**Growth hormone (GH) deficiency** occurs in approximately 1 in 4000 school-age children. These children demonstrate a **growth rate that is slow, usually falling away from the normal growth curve** (in contrast to constitutional delay where growth parallels the third to fifth percentile curve). On examination these children often appear younger than their stated age and frequently appear chubby (weight age > height age). **Bone ages are delayed**, indicating catch-up growth potential. GH screening tests include serum IGF-1 or somatomedin C and IGF-BP3. Confirmation often requires GH stimulation testing and interpretation by a pediatric endocrinologist. Replacement therapy involves recombinant GH injections several times per week until the child reaches full adult height.

**Clues that growth failure may be caused by an underlying condition** not already mentioned include **poor appetite, weight loss, abdominal pain or diarrhea, unexplained fevers, headaches or vomiting, weight gain out of proportion to height, or dysmorphic features.** Screening tests might include a CBC (anemia), ESR (chronic inflammatory diseases), electrolytes (acidosis or renal abnormalities), general health chemistry panel (hepatitis, liver dysfunction), urinalysis (infection, renal disease), thyroid function tests (hypothyroidism), IGF-1 and IGF-BP3 (GH deficiency), and, for girls, possibly chromosomal analysis (Turner syndrome). Children with growth failure who do not fall into another, more appropriate category are classified as having idiopathic short stature.

## COMPREHENSION QUESTIONS

- 21.1 An 8-year-old boy has short stature. He has begun to gain quite a bit of weight over the last year, has little or no energy, sleeps more than normal, and complains of being cold. His growth curve demonstrates that he has fallen from the 50th percentile to the 5th percentile for height, but his weight has increased to the 90th percentile. On examination, he is obese and has an immature facies, thin hair, and slow reflexes. Which of the following is the most appropriate course of action for this child?
- A. Order Epstein-Barr virus titers.
  - B. Measure thyroid function.
  - C. Reassure the mother that the child has normal prepubertal development.
  - D. Determine bone age.
  - E. Order a somatomedin C level.
- 21.2 A 16-year-old boy complains that he is the shortest boy in his class. He has a normal past medical history, and although always a bit small for age, he has really noticed that he has fallen behind his peers in the last 2 years. He is Tanner stage 3 and is at the 5th percentile for height. His father began puberty at the age of 16 and completed his growth at the age of 19; he is now 6 ft 2 in tall. His mother began her pubertal development at the age of 10 and had her first menstrual period at the age



of 13; her height is 5 ft 4 in. Which of the following is the single most appropriate first intervention?

- A. Chromosomal analysis
- B. Liver function studies
- C. Measurement of bone age
- D. Measurement of somatomedin C
- E. Pediatric endocrinology referral

21.3 A 17-year-old girl is 4 ft 10 in tall. Her father is 5 ft 10 in tall and her mother is 5 ft 5 in tall. Her past medical history is significant for lifelong short stature and cardiac surgery at the age of 1 year. She has never had a menstrual period. Which of the following is the most appropriate first action?

- A. Chromosomal analysis
- B. Referral to a pediatric endocrinologist
- C. Serum testosterone levels
- D. Thyroid function studies
- E. Ultrasonogram of the abdomen

21.4 You see a 14-year-old boy in the juvenile detention center where he is currently living for arson to an abandoned building. He is tall, slim, underweight, and appears to have especially long legs. His testes are small for age, and his phallus seems somewhat undersized. His mother reports that he had difficulty with reading, spelling, and mathematics early on, but now he has difficulty in all classes. Which of the following diagnostic tests is most likely to identify his problem?

- A. Chromosomal analysis
- B. Referral to pediatric endocrinology
- C. Serum testosterone levels
- D. Thyroid function studies
- E. Ultrasonogram of the abdomen

## ANSWERS

- 21.1 **B.** This child has classic symptoms of acquired hypothyroidism. A bone age would be delayed, but thyroid function studies are needed to make the diagnosis. Thyroid hormone replacement therapy should resolve these symptoms, and growth should resume normally.
- 21.2 **C.** This boy likely has constitutional growth delay, similar to that of his father. Bone age would be delayed, indicating potential growth. He eventually will enter puberty, but the psychosocial ramifications of remaining shorter and appearing more immature than his peers may warrant treatment. Monthly testosterone injections “jump start” the pubertal process without altering final growth potential; a pediatric endocrinologist might be required to assist.
- 21.3 **A.** Chromosomal analysis is likely to show Turner syndrome (TS) in this child with parents of normal height. The surgery might have been for coarctation of the aorta. Common TS features include female phenotype, short stature, sexual infantilism, streak gonads, broad chest, low hairline, webbed neck, and congenital lymphedema of the hands and feet. Some TS children benefit from GH therapy.
- 21.4 **A.** Boys with Klinefelter syndrome are tall for their age; the testes are smaller than normal and feel firm and fibrotic. Examination can reveal eunuchoid body habitus and reduced upper body-lower body segment ratio (a long lower segment). Diagnosis is established by karyotyping.
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## CLINICAL PEARLS

- Constitutional growth delay is a condition in which a healthy child’s growth is slower than expected and for whom at least one parent demonstrated a pubertal development delay but normal adult height (“late bloomers”). Growth parallels the 3rd or 5th percentile growth curve; bone age is delayed.
- Familial short stature is a condition in which a short child is born to short parents who had normal timing of their pubertal development. Growth parallels the 3rd or 5th percentile growth curve; bone age is normal.
- Idiopathic short stature includes children with short stature for whom a more appropriate diagnosis cannot be found.

- Growth hormone (GH) deficiency is a condition in which inadequate GH secretion results in growth failure, delayed bone age, and catch-up growth upon GH replacement.
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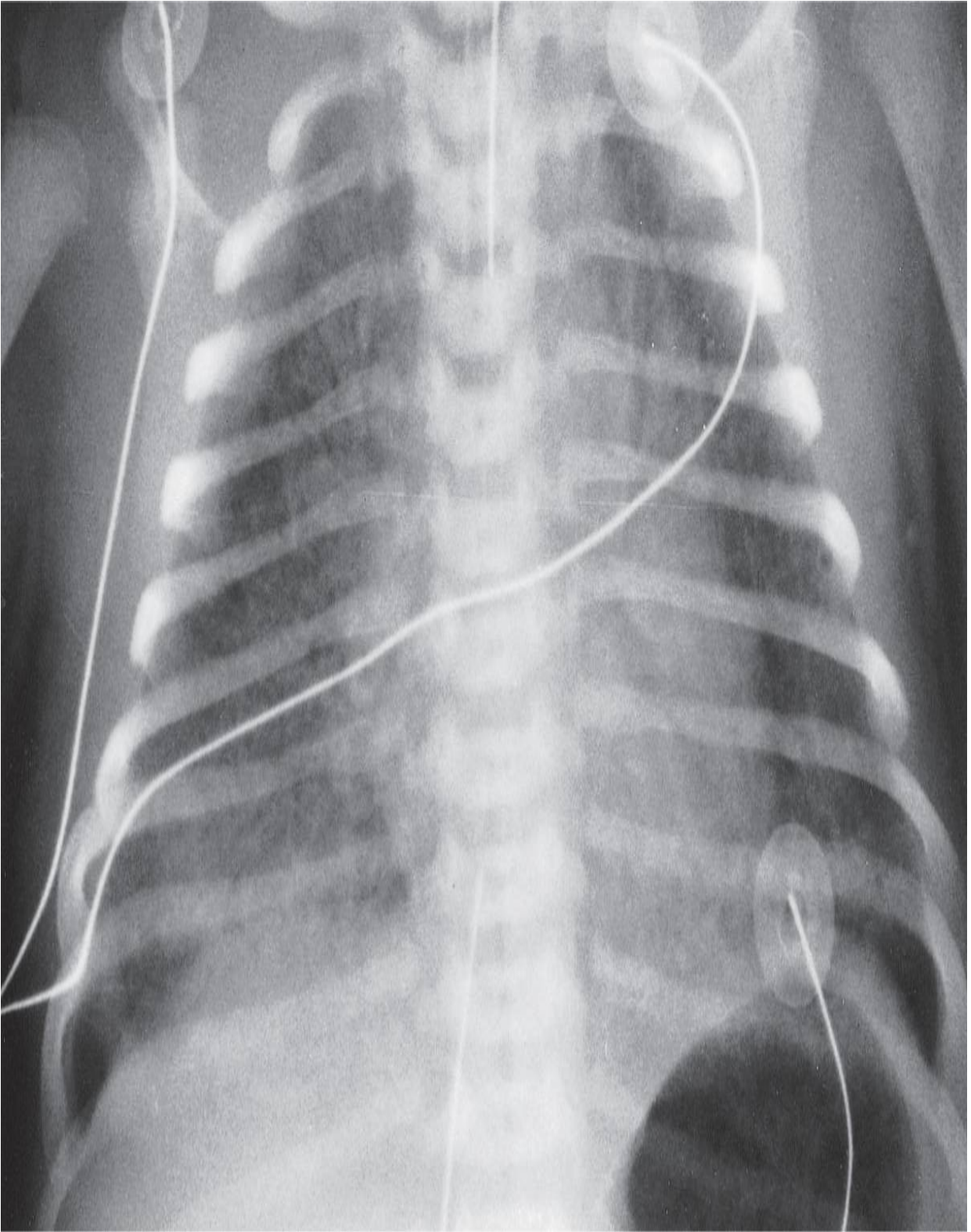
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## CASE 22

A 2800-g male is born at 36 weeks' gestation to a 19-year-old mother through vaginal delivery. Delivery occurred 19 hours after membrane rupture. The



mother's pregnancy was uncomplicated, but her prenatal records are not available at delivery. At 6 hours of age he is "breathing hard" and refusing to breast-feed. His respiratory rate is 60 breaths/min with "grunting." His temperature is 96.5°F (35.8°C), and his blood pressure is lower than normal. You ask the nurses to obtain a complete blood count (CBC) while you drive to the hospital from home. Upon arrival you confirm that he is in respiratory distress and that his perfusion is poor. The CBC demonstrates a white blood cell (WBC) count of 2500 cells/mm<sup>3</sup> with 80% bands. His radiograph is shown in [Figure 22-1](#).



**Figure 22-1.** Chest radiograph of an infant.

- What is the most likely diagnosis?

► What is the best therapy?

## ANSWERS TO CASE 22: **Group B Streptococcal Infection**

*Summary:* A 2800-g infant born by vaginal delivery at 36 weeks' gestation is found to have poor feeding, tachypnea, hypothermia, and poor perfusion at 6 hours of age.

- **Most likely diagnosis:** Group B *Streptococcus* (GBS) infection.
- **Best therapy:** Intravenous (IV) antibiotics (after addressing ABCs).

## ANALYSIS

### *Objectives*

1. Understand the common presentations of neonatal sepsis.
2. Understand the maternal risk factors for neonatal GBS infection.
3. Appreciate the variety of organisms responsible for neonatal infections.
4. Learn treatment options for the common neonatal infections.

### *Considerations*

The rapid symptom onset, the low WBC count with left shift, and the chest x-ray findings are typical for GBS pneumonia. At this point, management would include rapid application of the ABCs of resuscitation (maintain Airway, control Breathing, and ensure adequate Circulation), followed by rapid institution of appropriate antibiotics once cultures are obtained. Despite these measures, mortality from this infection is high.

APPROACH TO:

**Group B Streptococcal Infection**

## DEFINITIONS

**EARLY-ONSET SEPSIS SYNDROME:** Neonatal sepsis occurring in the first 6 days of life. The majority of infections (approximately 85%) occur in the first 24 hours of life, an additional 5% by approximately 48 hours, and the

remainder throughout the next 4 days. The infection source usually is microorganism acquisition from the mother's genitourinary tract.

**GROUP B *STREPTOCOCCUS* (GBS) COLONIZATION:** Infection with GBS limited to mucous membrane sites in a healthy adult; the gastrointestinal (GI) tract is the most common colonization reservoir.

**LATE-ONSET SEPSIS SYNDROME:** Neonatal sepsis usually occurring after approximately 7 days but before approximately 90 days of life. The infection source often is the caregiver's environment.

**INTRAPARTUM ANTIBIOTIC PROPHYLAXIS:** Intravenous penicillin or ampicillin given during labor to prevent newborn GBS disease.

## CLINICAL APPROACH

### *Signs and Symptoms of Sepsis*

The signs and symptoms of neonatal sepsis can be subtle and nonspecific, often overlapping with findings in other conditions, such as respiratory distress syndrome, metabolic disorders, intracranial hemorrhages, and traumatic deliveries. Temperature instability, tachypnea, hypotension, and bradycardia are common findings in sepsis and meningitis. **Overwhelming shock is manifested as pallor and poor capillary refill.** Neurologic findings of impaired level of consciousness, coma, seizures, bulging anterior fontanelle, focal cranial nerve signs, and nuchal rigidity are unusual, but when present hint at meningitis, a condition more commonly seen in late-onset disease. Examination findings seen frequently with pneumonia (more commonly seen in early-onset disease) include tachypnea, grunting, nasal flaring, retractions (costal or substernal), decreased breath sounds, and cyanosis.

### *Evaluation of the Potentially Septic Child*

Some neonatal sepsis laboratory findings can be nonspecific, including hypoglycemia, metabolic acidosis, and jaundice. The CBC often is used to help guide therapy, although the sensitivity and specificity of this test are low. Evidence of infection on CBC includes the following:

- Markedly elevated or low WBC counts

- Increased neutrophil count
- Increased immature to total neutrophil (I/T) ratios
- Thrombocytopenia with platelet counts less than 100,000/mm<sup>3</sup>

The C-reactive protein (an acute phase protein increased with tissue injury) can be elevated in septic infants; some use it as an adjunct to assess for neonatal sepsis.

**A blood culture is crucial for patients with suspected sepsis.** Some argue that the low meningitis incidence, especially in early-onset disease, does not warrant routine cerebral spinal fluid testing; rather, the test should be reserved for documented (positive cultures) or presumed (patients so sick that a full antibiotic course is to be given regardless of culture results) sepsis. Urine cultures usually are included for late-onset disease evaluation. Chest radiologic findings include segmental, lobar, or diffuse reticulogranular patterns, the latter easily confused with respiratory distress syndrome (lack of surfactant).

## ***Pathogens***

The organisms that commonly cause early-onset sepsis colonize in the mother's genitourinary tract and are acquired transplacentally, from an ascending infection or as the infant passes through the birth canal. **Specific organisms include GBS, *Escherichia coli*, *Haemophilus influenzae*, and *Listeria monocytogenes*.** Late-onset disease occurs when the infant becomes infected in the postnatal environment, such as from the skin, respiratory tract, conjunctivae, gastrointestinal tract, and umbilicus. For the hospitalized infant, bacteria sources include vascular or urinary catheters or contact with health-care workers. Organisms commonly seen to cause late-onset disease include coagulase-negative staphylococci, *Staphylococcus aureus*, *E coli*, *Klebsiella* sp, *Pseudomonas* sp, *Enterobacter* sp, *Candida*, GBS, *Serratia* sp, *Acinetobacter* sp, and anaerobes.

**Group B *Streptococcus* is the most common cause of neonatal sepsis from birth to 3 months.** Approximately 80% of cases occur as early-onset disease (septicemia, pneumonia, and meningitis) resulting from vertical transmission from mother to infant during labor and delivery. Respiratory signs (apnea, grunting respirations, tachypnea, or cyanosis) are the initial

clinical findings in more than 80% of neonates, regardless of the site of involvement, whereas hypotension is an initial finding in approximately 25% of cases. Other signs are similar to those associated with other bacterial infections described above.

Neonates with GBS meningitis rarely have seizures as a presenting sign, yet 50% develop seizures within 24 hours of infection. The median age at diagnosis of early-onset GBS infection is 13 hours, earlier than for the other bacterial infections described above. Clinical history and findings suggestive of early-onset GBS disease (rather than of a noninfectious etiology for pulmonary findings) include prolonged rupture of membranes, apnea, hypotension in the first 24 hours of life, a 1-minute Apgar score less than 5, and rapid progression of pulmonary disease.

**Factors associated with increased risk for early-onset GBS disease are rupture of membranes more than 18 hours before delivery, chorioamnionitis or intrapartum temperature greater than 100.4°F (38°C), previous infant with GBS infection, mother younger than 20 years, and low birth weight or prematurity (<37 weeks' gestation).** Mortality as a result of GBS disease is close to 10%. Major neurologic sequelae (cortical blindness, spasticity, and global mental retardation) occur in 12% to 30% of infants who survive meningitis.

The incidence of early-onset GBS infection decreased from 1.7 per 1000 live births in 1993 to 0.34-0.37 per 1000 live births in 2008. The decline is largely attributed to the widespread use of GBS risk-reduction guidelines. These guidelines recommend **screening women at 35 to 37 weeks' gestation and offering intrapartum antibiotic prophylaxis to those with risk factors or positive GBS cultures at 35 to 37 weeks' gestation.** Infants born at less than 35 weeks' gestation or born to women who received inadequate intrapartum prophylaxis sometimes undergo a limited evaluation that often includes a CBC and blood culture. The association of early antibiotic use with increased risk of late-onset serious bacterial infections remains under study.

## ***Treatment***

Treatment of suspected early-onset disease includes antibiotics directed at the common pathogens listed earlier, often consisting of a combination of IV aminoglycosides (gentamicin or tobramycin) and penicillin (often ampicillin). For patients with late-onset disease, therapy often consists of  $\beta$ -lactamase-

resistant antibiotics (such as vancomycin) and second- or third-generation cephalosporins.

For early- and late-onset disease, antibiotic coverage is adjusted depending on the organism identified and the organism's specific antibiotic sensitivities.

Antibiotics are continued for at least 48 to 72 hours. If cultures are negative and the patient is well, antibiotics often are stopped. **For infants presenting with convincing signs and symptoms of sepsis, antibiotics may be continued even with negative cultures.** For infants with positive cultures, therapy continues for 10 to 21 days depending on the organism and the infection site. Close observation for signs of antibiotic toxicity is important for all infants.

## COMPREHENSION QUESTIONS

- 22.1 A newborn infant was born at home. At 2 days of life he has puffy, tense eyelids, red conjunctivae, a copious purulent ocular discharge, and chemosis. Which of the following is the most likely diagnosis?
- A. Chemical conjunctivitis
  - B. Chlamydial conjunctivitis
  - C. Dacryocystitis
  - D. Gonococcal ophthalmia
  - E. Pneumococcal ophthalmia
- 22.2 A term 3500-g female delivered by cesarean section develops a respiratory rate of 70 breaths/min and expiratory grunting at 1 hour of life. She has good tone, good color, and a strong suck. Which of the following is the most appropriate next intervention?
- A. Intubation and suctioning below the vocal cords
  - B. Administration of surfactant
  - C. Initiation of antibiotic therapy
  - D. Swallow study and upper GI series
  - E. Observation for a period of several hours

- 22.3 A term infant is born to a 23-year-old known HIV-positive mother. The mother has been followed closely during the pregnancy, and she has been taking antiretroviral medications for the weeks prior to the delivery. Routine management of the healthy infant should include which of the following?
- A. Administration of intravenous immunoglobulin to the baby to decrease the risk of perinatal HIV infection
  - B. Admission to the neonatal intensive care unit for close cardiovascular monitoring
  - C. Beginning a course of zidovudine for the infant
  - D. Chest radiographs to evaluate for congenital *Pneumocystis carinii* E. HIV enzyme-linked immunosorbent assay (ELISA) on the infant to determine if congenital infection has occurred
- 22.4 A 2150-g infant is delivered at 34 weeks' gestation. The mother had prenatal care in Mexico and says she had no problems. Her highest temperature during labor was 100.8°F (38.2°C). The amniotic fluid had a brown-stained appearance. At birth the infant had a diffuse erythematous pustular rash, pallor, poor feeding, tachypnea, and cyanosis. His CBC indicates marked monocytosis. He dies at 4 hours of age, soon after initiation of antibiotics. He most likely had which of the following?
- A. Congenital syphilis
  - B. Congenital varicella
  - C. Disseminated herpes
  - D. GBS disease
  - E. Listeriosis

## ANSWERS

- 22.1 **D.** The time of symptom onset in a neonate with conjunctivitis can be helpful. Chemical conjunctivitis that is self-limited and presents within 6 to 12 hours of birth is the result of ocular prophylaxis irritation. Gonococcal conjunctivitis usually occurs within 2 to 5 days of birth and is the most serious of the bacterial infections; prompt and aggressive



topical treatment and systemic antibiotics can prevent serious complications such as corneal ulceration, perforation, and resulting blindness. Parents are treated for gonococcal disease to prevent a child's reinfection. Chlamydial conjunctivitis often presents 5 to 14 days after birth and often is treated with systemic erythromycin (in part to reduce the infant's risk of chlamydial pneumonia at 2-3 months of age). The risks of oral erythromycin treatment must be weighed against the increased risk of hypertrophic pyloric stenosis, a condition associated with oral erythromycin use in children. Both parents of a child with chlamydial conjunctivitis also are treated.

- 22.2 E. Transient tachypnea of the newborn is a respiratory condition resulting from incomplete evacuation of fetal lung fluid in full-term infants. It occurs more commonly with cesarean deliveries and usually disappears within 24 to 48 hours of life. Often no treatment is indicated unless the infant requires low amounts of supplemental oxygen. Antibiotics would be indicated for a child for whom pneumonia would be suspected; these children usually do not have a vigorous suck as outlined in the question. Intubation and suctioning below the vocal folds hints at meconium aspiration; the intubation would appropriately be accomplished in the delivery room and not hours later. The barium swallow and upper GI series might be helpful to identify a tracheoesophageal fistula. Exogenous surfactant is used for premature infants for whom surfactant deficiency is suspected.
- 22.3 C. HIV transmission from mother to infant has decreased dramatically over the last 20 years, probably as a result of perinatal antiretroviral administration to the mother and a zidovudine course to the exposed infant. Transplacentally transmitted maternal HIV antibodies will result in a positive neonatal ELISA; it is not a useful test for determining newborn infection. Intravenous immunoglobulin has not been shown to have a role in decreasing perinatal transmission. Healthy infants born to HIV-infected mothers require neither special monitoring nor routine radiographs.
- 22.4 E. *Listeria* is a gram-positive rod isolated from soil, streams, sewage, certain foods, silage, dust, and slaughterhouses. The foodborne transmission of disease is related to soft-ripened cheese, whole and 2% milk, undercooked chicken and hot dogs, raw vegetables, and shellfish.

The newborn infant acquires the organism transplacentally or by aspiration or ingestion at delivery. The mortality rate of early-onset disease is approximately 30%.

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## CLINICAL PEARLS

- Sepsis in the neonate can present with nonspecific findings of temperature instability, tachypnea, poor feeding, bradycardia, hypotension, and hypoglycemia.
  - Early-onset neonatal infection (occurring in the first 6 days of life) usually is caused by organisms of the maternal genitourinary system, including group B *Streptococcus* (GBS), *E coli*, *H influenzae*, and *L monocytogenes*. Pneumonia and sepsis are common presentations; GBS is the leading cause.
  - Late-onset neonatal infection (occurring between 7 and 90 days of life) is often caused by organisms found in the infant's environment, including coagulase-negative staphylococci, *S aureus*, *E coli*, *Klebsiella* sp, *Pseudomonas* sp, *Enterobacter* sp, *Candida*, GBS, *Serratia* sp, *Acinetobacter* sp, and anaerobic bacteria.
  - Treatment of early-onset neonatal infection usually includes penicillin and an aminoglycoside, whereas treatment of late-onset disease consists of a  $\beta$ -lactamase-resistant antibiotic (such as vancomycin) and often a third-generation cephalosporin.
  - The incidence of early-onset GBS infection is decreasing, likely as a result of the widespread implementation of GBS risk-reduction guidelines.
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## CASE 23

A 3-month-old boy is discovered not breathing in his crib this morning. Cardiopulmonary resuscitation was begun by the parents and was continued by paramedics en route to the hospital. You continue to try to revive the child in the emergency center, but pronounce him dead after 20 minutes of resuscitation. You review the history with the family and examine the child, but you are unable to detect a cause of death.

- ▶ How should you manage this situation in the emergency department?
- ▶ What is the most likely diagnosis?
- ▶ What is the next step in the evaluation?

## ANSWERS TO CASE 23: Sudden Infant Death Syndrome

*Summary:* A 3-month-old boy discovered not breathing by his parents.

- **First step:** Tell the boy's parents that despite everyone's best efforts, their son has died. Ask the parents if they would like you to call a friend, family member, religious leader, or other support person. Provide them with a quiet room where they can be left alone.
- **Most likely diagnosis:** Sudden infant death syndrome (SIDS) is the most likely diagnosis, assuming that the parents' story is true. Infanticide must be considered, as well as the possibility of an underlying congenital or metabolic disorder.

- **Next step:** Discuss with the parents that routine protocol is followed after an unexplained infant death. A coroner will perform an autopsy and police investigators will examine the parents' home for clues related to the death. Emphasize that these measures can help to bring closure for the family and may yield important information for preventing future child deaths should the couple have more children.

## ANALYSIS

### *Objectives*

1. Know the definition of SIDS.
2. Know the factors that are associated with SIDS.
3. Know how to counsel parents about SIDS risk-reducing measures.

### *Considerations*

Sudden infant death syndrome is one of the most tragic and frustrating medical diagnoses. When the family is in the emergency center, other possible causes of death (eg, child abuse or inherited disorders) cannot be excluded. Your role is to remain objective about these other possibilities yet sympathetic to the parents' grieving. As always, meticulous documentation of the history and physical examination findings is imperative.

### APPROACH TO:

#### **Sudden Infant Death Syndrome**

## DEFINITIONS

**APPARENT LIFE-THREATENING EVENT (ALTE):** Observations and events perceived by a caregiver as life-threatening. By definition, the event is observed. Myriad conditions may be responsible, including cardiac, respiratory, central nervous system (CNS), metabolic, infectious, and gastrointestinal causes. In approximately 50% of cases a cause is never known.

**APNEA:** Cessation of breathing for at least 20 seconds that may be accompanied by bradycardia or cyanosis. Recurrent episodes of apnea related

to immaturity may occur in premature infants, but usually resolve by 37 weeks postgestational age.

**SUDDEN INFANT DEATH SYNDROME (SIDS):** The sudden death of an infant that cannot be explained by results of a postmortem examination, death scene investigation, and historical information.

## CLINICAL APPROACH

**Sudden infant death syndrome is the most common cause of death in infants between the ages of 1 week and 1 year.** The majority of SIDS deaths occur between 1 and 5 months of age, with a **peak incidence between 2 and 4 months** of age; it is **more common in winter**. SIDS is more common among **African-American and Native-American infants**; whether these latter associations result from ethnicity or reflect other environmental factors is unclear.

No cause of SIDS has been identified. Epidemiologic studies suggest that the following are independent SIDS risk factors: **prone or side sleep position**, sleeping on a **soft surface**, **bed sharing**, pre- and postnatal exposure to tobacco smoke, maternal prenatal use of opiates, **over-heating**, late or no prenatal care, young maternal age, **prematurity** and/or low birth weight, and male gender. The incidence of SIDS has decreased dramatically in areas with public education campaigns targeted at limiting prone sleep positioning. The investigation of the unexpected infant death includes a clinical history, a postmortem examination, and a death scene investigation. In some infants, autopsy reveals mild pulmonary edema and scattered intrathoracic petechiae; these findings are supportive but not diagnostic of SIDS.

Explainable causes of sudden infant death can be divided into **congenital and acquired conditions**. **Congenital conditions** include **cardiac anomalies** (arrhythmia, congenital heart disease), **metabolic disorders**, and **CNS etiologies**. **Acquired causes** include infection and both **accidental and intentional trauma**. Infants who have experienced an ALTE may be at risk for sudden death. The evaluation of an ALTE infant is guided by the history and physical examination. **A report of feeding difficulties or emesis leads to consideration of swallowing studies**, whereas **unusual posturing or movements leads to an electroencephalogram**. A complete blood count and serum bicarbonate level obtained close to the time of the event may help to

uncover an infectious or metabolic etiology. An electrocardiogram may be considered to look for prolonged QT syndrome or other cardiac anomaly. Documented cardiorespiratory monitoring and polysomnography can be helpful in some cases.

In the past, infants with a history of apnea were thought to be at risk for SIDS, but more recent epidemiologic research has refuted this hypothesis. Siblings of infants who have died of SIDS have been reported to potentially be at increased risk of SIDS themselves, but the role of a possible genetic susceptibility versus environmental factors and unrecognized infanticide in these cases is unclear.

## COMPREHENSION QUESTIONS

- 23.1 Which of the following infants most warrants home cardiorespiratory monitoring?
- A. A healthy 3-month-old infant, born at term, whose weight is at the 5th percentile
  - B. A healthy infant, born at 29 weeks' gestation, whose weight is at the 50th percentile
  - C. A 5-month-old infant with a history of recurrent bouts of wheezing
  - D. A premature infant with recurrent apnea and bradycardia
  - E. A healthy term infant whose older sibling died of SIDS
- 23.2 A pregnant woman comes to you for a prenatal visit. As her family pediatrician, your advice to her should include which of the following statements about reducing the risk of SIDS?
- A. Reduce the infant's exposure to tobacco smoke, and always place the baby in the supine position when she sleeps.
  - B. Always keep the baby in the prone position, even while awake.
  - C. Administer supplemental infant vitamins.
  - D. Attempt to make breast milk the infant's primary source of nutrition.
  - E. Protect the infant from people who are ill.
- 23.3 Which of the following statements about the environment to reduce SIDS is accurate?

- A. Infants should sleep in the same bed as the parent or on their chest so they can be closely monitored for apnea.
  - B. Infants should sleep on a firm mattress with no accompanying soft bedding or objects, including no devices advertised to maintain the sleep position.
  - C. Pacifiers should be avoided as they can obstruct the baby's airflow during respiration.
  - D. Infants placed to sleep on their backs will have more episodes of plagiocephaly, reflux, choking, and ALTEs.
  - E. Infants should be given acetaminophen before their scheduled vaccines in order to prevent an undetected febrile seizure and resulting SIDS.
- 23.4 The investigation of an unexpected infant death includes a history, a postmortem examination, and which of the following?
- A. DNA studies
  - B. An arterial blood gas measurement
  - C. A venous blood gas measurement
  - D. A death scene investigation
  - E. Stool studies

## ANSWERS

- 23.1 **D.** Home cardiorespiratory monitoring has not been shown to decrease the incidence of SIDS. Monitoring is recommended for symptomatic premature infants (ie, those with apnea and bradycardia), but can safely be discontinued by 43 weeks postgestational age in most cases. Monitoring may also be warranted for children with certain underlying chronic conditions, such as those with chronic lung disease. It is not recommended for the infants in choices A, B, or C. The occurrence of a genetic susceptibility to SIDS within a family is thought to be exceedingly rare.
- 23.2 **A.** Although your advice to this woman might also include choices C, D, and E, these measures have not been shown to reduce the infant's risk of SIDS.



- 23.3 **B.** The decline in SIDS from 20 years ago has been attributed to the change in sleep position. Recently, pacifier use has been identified as a protective measure. Infants who have died of SIDS have been less likely to have been immunized. While there has been an increase in positional plagiocephaly since the Back to Sleep campaign, it can be avoided with adequate tummy time, frequent upright holding, and alternating the crib orientation. The other events have not occurred with increased incidence.
- 23.4 **D.** A death scene investigation is crucial to rule out trauma, both intentional and accidental.
- 

### CLINICAL PEARLS

- Sudden infant death syndrome (SIDS) is a diagnosis of exclusion assigned only after the postmortem investigation, postnatal history, and crime scene investigation fail to yield another explanation.
  - Prone sleep position and exposure to cigarette smoke are significant risk factors for SIDS.
  - Apparent life-threatening events (ALTE) are observed occurrences that can be caused by myriad etiologies.
  - Apnea of prematurity is not a risk factor for SIDS.
- 

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## CASE 24

A 3-month-old boy in respiratory distress presents to the emergency department. It is January, so you suspect the coarse wheezes heard on chest auscultation by the triage nurse are the result of a viral respiratory infection; you approve the administration of aerosolized albuterol. About 20 minutes later you are able to obtain from the mother a more complete history. She tells you the baby began having intermittent wheezing approximately 4 weeks ago and the episodes have become progressively worse. You then listen to the infant and discover that, in addition to wheezes, a holosystolic murmur can be heard along the left sternal border. The oxygen saturation obtained at triage was normal.

- What is the most likely diagnosis?
- What is the treatment for this condition?

ANSWERS TO CASE 24: **Ventricular Septal Defect**

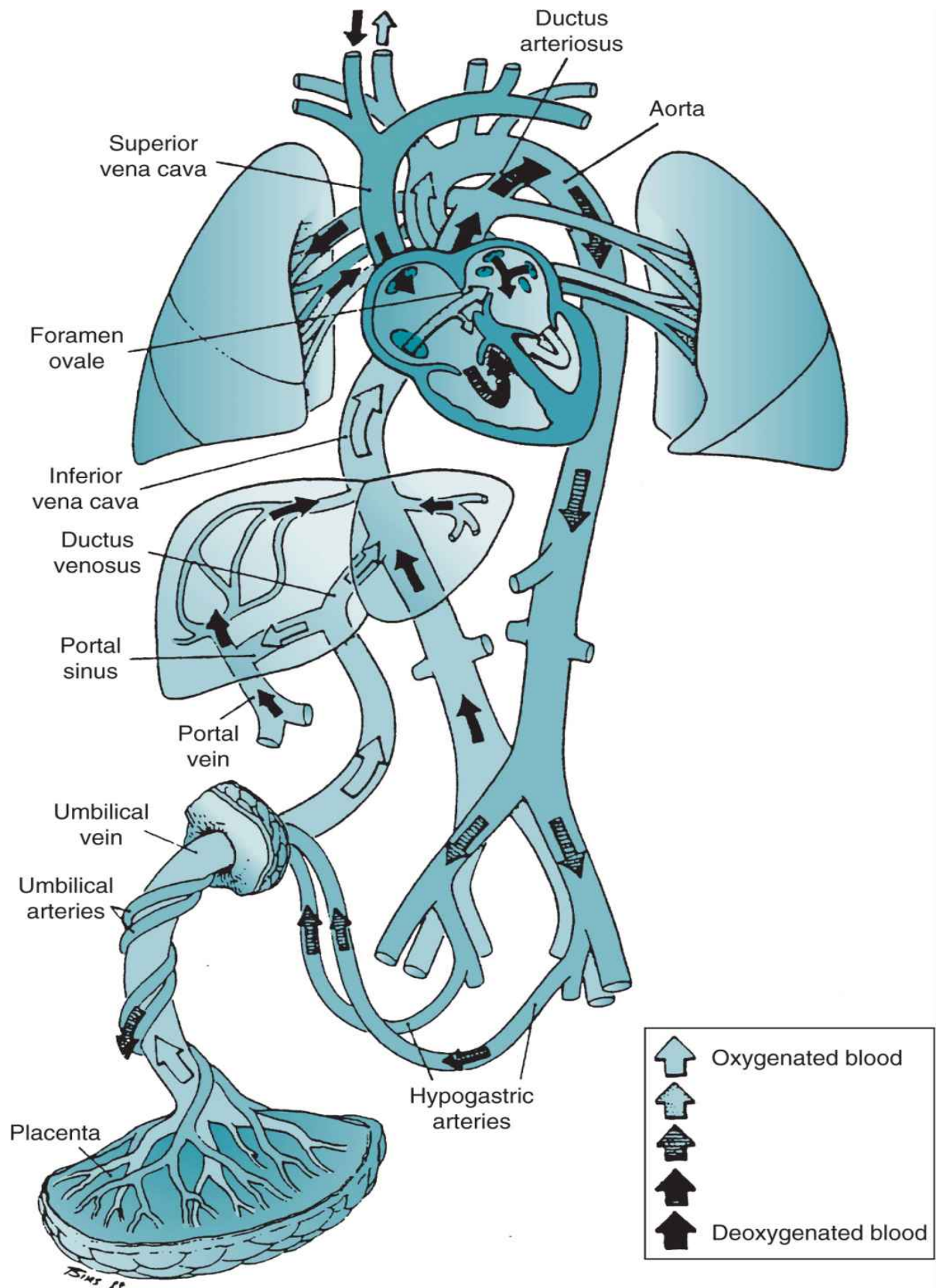
*Summary:* A 3-month-old infant presents with respiratory distress, wheezing, and a soft holosystolic heart murmur. His symptoms began 4 weeks ago and have become progressively worse.

- **Most likely diagnosis:** Ventricular septal defect (VSD).
- **Treatment:** Medical management, and possible eventual surgical closure.

## ANALYSIS

### *Objectives*

1. Recognize the presenting signs and symptoms of VSD.
2. Know the major acyanotic congenital heart lesions.
3. Be familiar with the fetal circulation ([Figure 24-1](#)).



**Figure 24-1.** Fetal circulation. (Reproduced, with permission, from Cunningham G, Leveno KL, Bloom SL. *Williams Obstetrics*. 22nd ed. New York, NY: McGraw-Hill; 2005.)

### ***Considerations***

An acyanotic heart lesion is suspected in this child who has a new heart murmur without cyanosis. The fall in pulmonary vascular resistance that occurs in the weeks following birth allows blood to flow from left to right across a VSD, resulting in an audible murmur by 2 to 6 months of life. This child's VSD is of sufficient size to result in congestive heart failure. Unlike the cause of wheezing in most of the other infants presenting to the emergency department in winter, this child's respiratory distress is not due to a viral respiratory infection.

APPROACH TO:

**Acyanotic Heart Lesions**

## **DEFINITIONS**

**EISENMENGER SYNDROME:** Pulmonary hypertension (HTN) resulting in right-to-left shunting of blood. This may occur with large ventricular septal defects (VSDs), atrioventricular canal lesions, and patent ductus arteriosus (PDA).

**LEFT-TO-RIGHT SHUNT:** Flow of blood from the systemic circulation into the pulmonary circulation across an anomalous connection, such as a PDA. Such lesions result in pulmonary congestion, but they typically do not cause cyanosis. Systemic hypoperfusion may result if the cause is an obstructive lesion (such as pulmonic or aortic valve stenosis, coarctation of the aorta).

**WIDENED PULSE PRESSURE:** An increase in the difference between systolic and diastolic pressures, resulting in a bounding arterial pulse. Many conditions may cause this finding, including fever, hyperthyroidism, anemia, arteriovenous fistulas, and PDA.

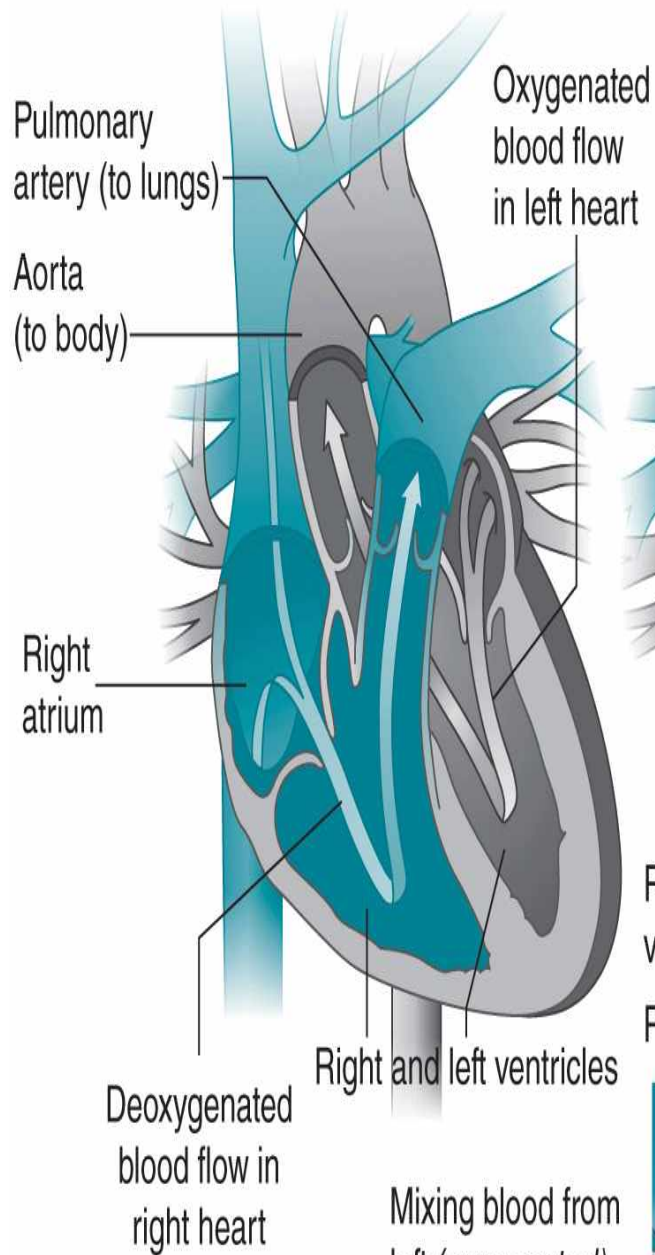
## **CLINICAL APPROACH**

**Congenital cardiac defects are first categorized according to the presence of cyanosis.** They are then further classified according to chest radiograph findings of increased, normal, or decreased pulmonary vascular markings, and then finally according to ventricular forces indicated on electrocardiography. **The majority of acyanotic lesions result in a change in volume load, usually from the systemic circulation to the pulmonary circulation (so called left-to-right shunt).** Left untreated, defects that affect volume load can eventually result in increased pulmonary vascular pressure, causing reversal of blood flow across the defect and clinical cyanosis. Other forms of acyanotic defects cause changes in pressure; this group includes pulmonic and aortic valve stenosis and coarctation of the aorta.

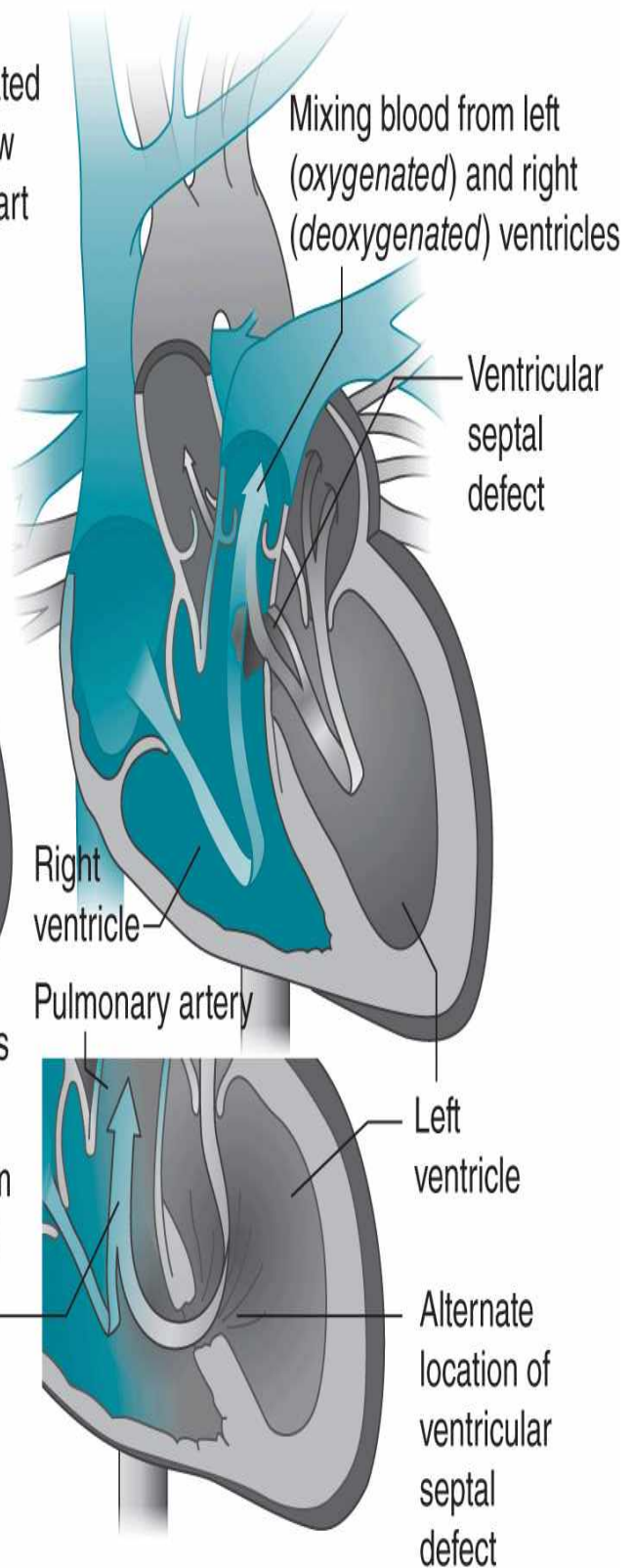
**Ventricular septal defect is the most common heart lesion in children,** affecting 3 to 6 of every 1000 live term births ([Figure 24-2](#)). The majority of VSDs occur in the membranous portion of the septum, and small VSDs with minimal left-to-right shunts are the most common. Children with **small VSDs** usually are asymptomatic, and a **harsh, left lower sternal border holosystolic murmur is detected on physical examination.** The **murmur of a large VSD may be less harsh** because of the absence of a significant pressure gradient across the defect. Large lesions are accompanied by **dyspnea, feeding difficulties, growth failure, and profuse perspiration,** and they may lead to recurrent infections and **cardiac failure.** Infants with large VSDs generally are not cyanotic, but they may become dusky during feeding or crying. A VSD may not be detected in the first few weeks of life because of high right-sided pressures but become audible as pulmonary vascular resistance drops and left-to-right shunting of blood increases across the defect. In children with significant VSDs, chest radiography shows cardiomegaly and pulmonary vascular congestion, and the electrocardiogram (ECG) shows biventricular hypertrophy.



**A** Normal heart



**B** Hearts with ventricular septal defects



**Figure 24-2.** Image A shows the structure and blood flow inside a normal heart. Image B shows two common locations for a ventricular septal defect. The defect allows oxygen-rich blood from the left ventricle to mix with oxygen-poor blood in the right ventricle. (From the National Institutes of Health. <http://www.nhlbi.nih.gov/health/health-topics/topics/chd/types.html> [accessed 09/07/11].)

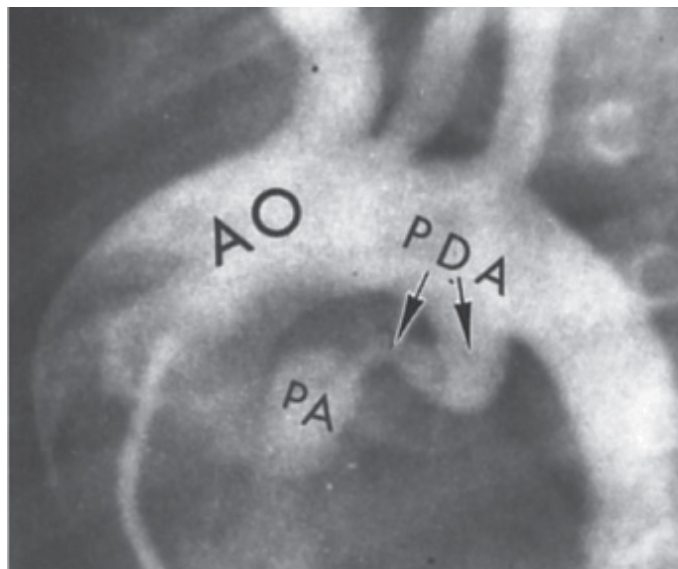
Most small VSDs close spontaneously by 6 to 12 months of life, especially if they occur in the muscular septum. Medical management is reserved for infants who are symptomatic from larger VSDs. Medications include diuretics (eg, furosemide, chlorothiazide) and afterload reduction agents (eg, an angiotensin-converting enzyme inhibitor) and sometimes digoxin. Affected infants also need adequate caloric intake, usually 140 kcal/kg/d, and may require feeding by nasogastric or gastrostomy tubes. When monitoring children with large VSDs, one should not be misled by a softening murmur, as this may herald pulmonary vascular disease or infundibular stenosis rather than closure of the defect.

Most children with large VSDs develop pulmonary vascular resistance after 1 year of age, although it can occur early; children with trisomy 21 are at particular risk of early disease. Children with persistently large shunts after 1 year of age usually undergo surgical closure, as one-third of these children have irreversible pulmonary vascular disease by 2 years of age (**Eisenmenger syndrome**).

Other acyanotic congenital heart lesions include **PDA**, atrial septal defects (ASDs), and atrioventricular septal defects. **Patent ductus arteriosus is most commonly seen in preterm infants**, but it also occurs in term infants. **In utero, the ductus arteriosus shunts blood from the quiescent lungs through the pulmonary artery to the descending aorta.** Shortly after birth, pulmonary resistance begins to fall, and vasoconstriction of the ductus occurs. **Ductus closure in term infants usually occurs within 10 to 15 hours of birth and almost always by 2 days.** Closure is delayed in premature infants, perhaps as a result of impaired vasoconstrictor response to increased oxygen tension. Failure of the ductus to close allows shunting of blood from the systemic circulation to the pulmonary circulation, with resultant myocardial stress, pulmonary vascular congestion, and respiratory difficulty. **A small PDA usually results in no symptoms but is still closed medically (usually with indomethacin) or surgically (if medical therapy fails or is**



**contraindicated**) due to risk of infective endarteritis and paradoxical emboli. An infant with a **large PDA** typically has a **systolic or continuous “machinerylike” heart murmur**, an active precordium, and a **widened pulse pressure**. Closure is accomplished to treat heart failure and prevent Eisenmenger syndrome. Occasionally, a PDA is present in association with another congenital cardiac lesion and may be difficult to detect. For patients with coarctation or interruption of the aortic arch, a PDA is vital to maintaining blood flow to the systemic circulation. Likewise, a PDA in the presence of an obstructed pulmonic valve is essential for providing blood flow to the lungs ([Figure 24-3](#)). Such lesions are called *ductus dependent*, and the PDA patency is maintained with an infusion of prostaglandin E.



**Figure 24-3.** Angiography of persistent patent ductus arteriosus (PDA). AO, aorta; PA, pulmonary artery. (Reproduced, with permission, from Rudolph CD, Rudolph AM, Hostetter MK, Lister G, Siegel NJ, eds. *Rudolph's Pediatrics*. 21st ed. New York, NY: McGraw-Hill; 2003:1819.)

**Children with ASDs often are asymptomatic** and the lesion discovered inadvertently on routine physical examination. **Large defects may cause mild growth failure and exercise intolerance** not appreciated except in retrospect after defect closure. Physical findings include a **widely split second heart sound that does not vary with respiration** (“fixed splitting”), and a systolic murmur at the left upper and midsternal borders caused by high-volume blood flow from the right ventricle into the normal pulmonary artery; the murmur is not blood flowing across the ASD itself. A lower left sternal border diastolic

murmur produced by increased flow across the tricuspid valve may be present. The chest radiograph reveals an enlarged right atrium, right ventricle, and pulmonary artery and increased pulmonary vascularity; ECG shows right ventricular hypertrophy and sometimes right-axis deviation. **Atrial septal defects are well tolerated during childhood but can lead to pulmonary HTN in adulthood or atrial arrhythmias from atrial enlargement.** Infective endocarditis is rare; routine prophylaxis is not recommended. An isolated patent foramen ovale usually is not clinically significant and is not considered an ASD.

**Atrioventricular septal defect** (also known as AV canal or endocardial cushion defect) consists of a contiguous atrial and ventricular septal defect as well as abnormal AV (ie, mitral and tricuspid) valves. This acyanotic lesion requires correction in infancy to prevent cardiac failure and associated complications. A systolic murmur of large pulmonary flow is present, and a lower left sternal border diastolic murmur is heard. The second heart sound may be widely split. The chest radiograph and ECG show cardiac enlargement; pulmonary vascularity is increased on the chest film.

Left untreated, these children develop **cardiac failure, growth failure, and recurrent pulmonary infections in infancy.** Pulmonary HTN develops with eventual right-to-left shunting and cyanosis. Surgical correction is performed in infancy.

## COMPREHENSION QUESTIONS

- 24.1 A 2-month-old girl with Down syndrome is noted to have a systolic and a diastolic heart murmur, and the second heart sound is split. The liver edge is palpable 4 cm below the right costal margin. Her mother reports that lately the baby has been sweaty and sometimes blue around the mouth when she nurses, and she seems to be eating less than previously. Her electrocardiogram (ECG) shows a superiorly oriented QRS frontal plane axis with counterclockwise depolarization pattern and right ventricular hypertrophy. Which of the following is the most likely diagnosis?
- A. Atrial septal defect
  - B. Atrioventricular canal defect

- C. Patent ductus arteriosus
- D. Patent foramen ovale
- E. Ventricular septal defect

24.2 A 1000-g boy, delivered at 29 weeks' gestation, is admitted to the neonatal intensive care unit, where he receives routine care. He does well until day 5 of life, when he develops an increased respiratory rate, mild subcostal retractions, and a widened pulse pressure, but no cyanosis or increased oxygen requirement. A continuous murmur is heard along the left sternal border. Chest radiography shows pulmonary vascular congestion. Which of the following medications may best relieve his symptoms?

- A. Albuterol
- B. Racemic epinephrine
- C. Indomethacin
- D. Digoxin
- E. Furosemide

24.3 A 12-month-old boy with a stable but moderate-size ventricular septal defect presents to the pediatric dentist for cleaning and management of his multiple caries. Prior to the procedure, he should receive which of the following?

- A. Acetaminophen
- B. Amoxicillin
- C. Digoxin
- D. Ditropan
- E. None of the above

24.4 A previously healthy term infant suddenly develops respiratory distress on day 3 of life. An echocardiogram reveals coarctation of the aorta. Which of the following is the most appropriate treatment for immediate stabilization of this infant?

- A. Digoxin
- B. Furosemide

- C. Albuterol
- D. Racemic epinephrine
- E. Prostaglandin therapy

## ANSWERS

- 24.1 B.** Atrioventricular canal defect is common among children with Down syndrome. This infant's symptoms and clinical findings are most consistent with this diagnosis. While a simple VSD is common in patients with Down syndrome, the multitude of heart murmurs and ECG findings make this answer less likely.
- 24.2 C.** A noncyanotic heart lesion is suspected in this child who has a new heart murmur without a corresponding increase in oxygen requirements. The murmur, not heard at birth, becomes evident after the pulmonary vascular resistance falls. His age, history, and physical findings are consistent with a patent ductus arteriosus (PDA). Indomethacin or surgical closure is used to treat this condition.
- 24.3 E.** The guidelines for the use of prophylactic antibiotics are updated frequently by the American Heart Association. Among those currently recommended to receive antibiotic prophylactic treatment are patients for whom any heart infection would result in the highest incidence of adverse outcome: previous history of endocarditis, prosthetic valve or material for repair, heart transplant patients, and severe or partially repaired cyanotic congenital heart defects.
- 24.4 E.** This infant's symptoms started when his ductus arteriosus began to close. Prostaglandin therapy can reverse this process in the short-term. Surgery or catheterization techniques provide definitive repair.
- 

## CLINICAL PEARLS

- Acyanotic heart lesions are characterized by shunting of blood from the systemic circulation to the pulmonary circulation ("left-to-right shunt").
- The most common congenital acyanotic heart lesion is the ventricular septal defect. Patent ductus arteriosus, atrial septal defect, and arteriovenous canal are other left-to-right shunt lesions.

- Left-to-right shunts eventually can reverse direction (right-to-left) and cause cyanosis if pulmonary hypertension develops (Eisenmenger syndrome).
- 

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## CASE 25

A term 3700-g boy was delivered vaginally without complications. He breast-feeds well, voids, and passes meconium in the first 12 hours of life. At 15 hours of life he is no longer interested in feeding and appears dusky. His

respiratory rate is 65 breaths/min, his oxygen saturation on pulse oximetry is 80%, and his capillary refill is 3 seconds. No heart murmur is audible, but a loud single second heart sound is noted.

- ▶ What is the most likely diagnosis?
- ▶ What is the best management for this condition?

### ANSWERS TO CASE 25: **Transposition of the Great Arteries**

*Summary:* A healthy-appearing term infant suddenly loses interest in feeding and develops cyanosis, hypoxia, poor peripheral perfusion, and tachypnea. Cardiac examination reveals a loud single second heart sound and no murmur.

- **Most likely diagnosis:** Cyanotic congenital heart disease (CHD), likely transposition of the great arteries (TGA).
- **Best initial management:** Administer prostaglandin E<sub>1</sub> to maintain patency of the ductus arteriosus.

## ANALYSIS

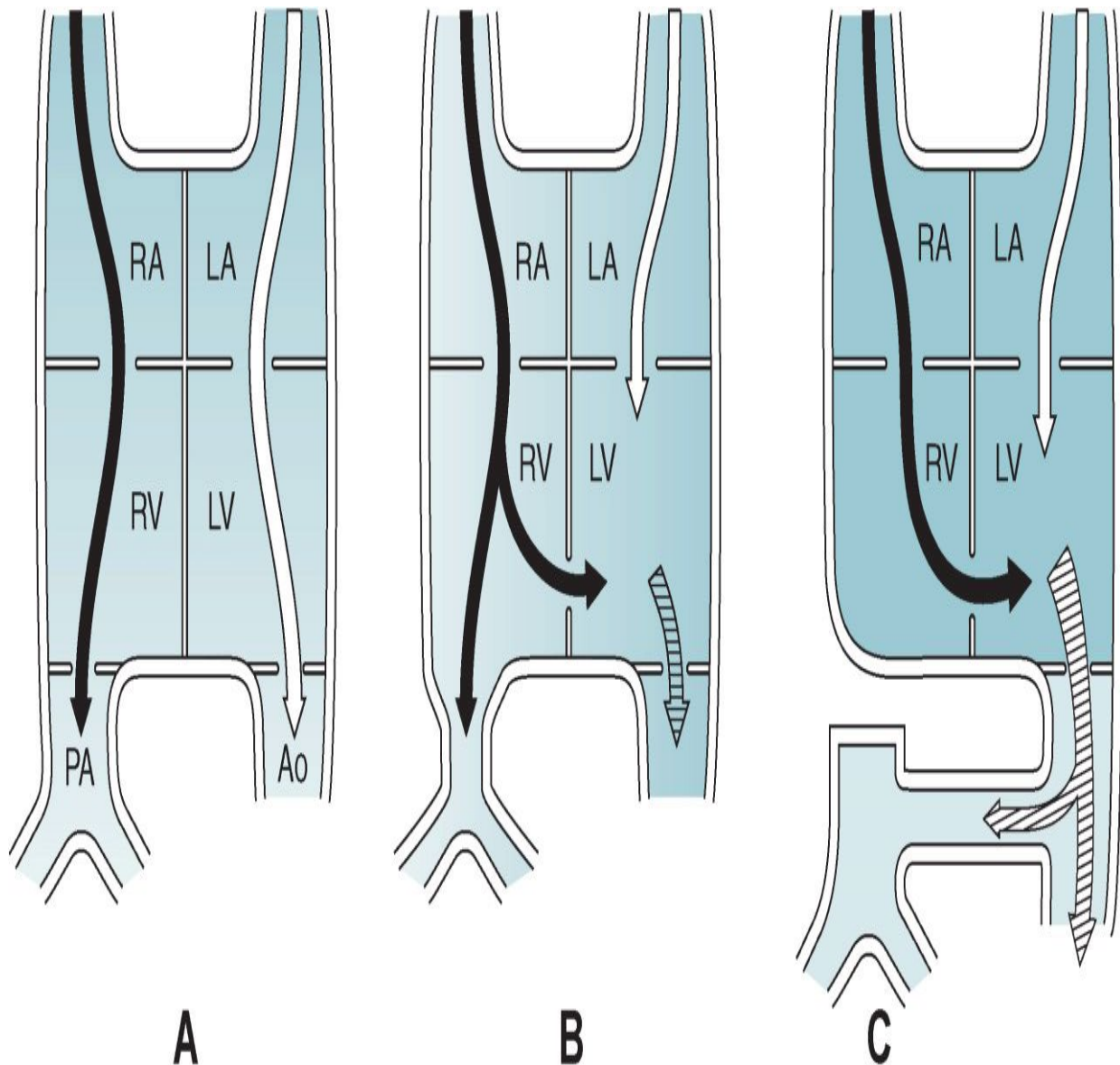
### *Objectives*

1. Know the major types of cyanotic CHD and their most common clinical presentations.
2. Understand why some types of CHD result in cyanosis whereas others do not.
3. Understand the need to maintain ductus arteriosus patency in some types of CHD.

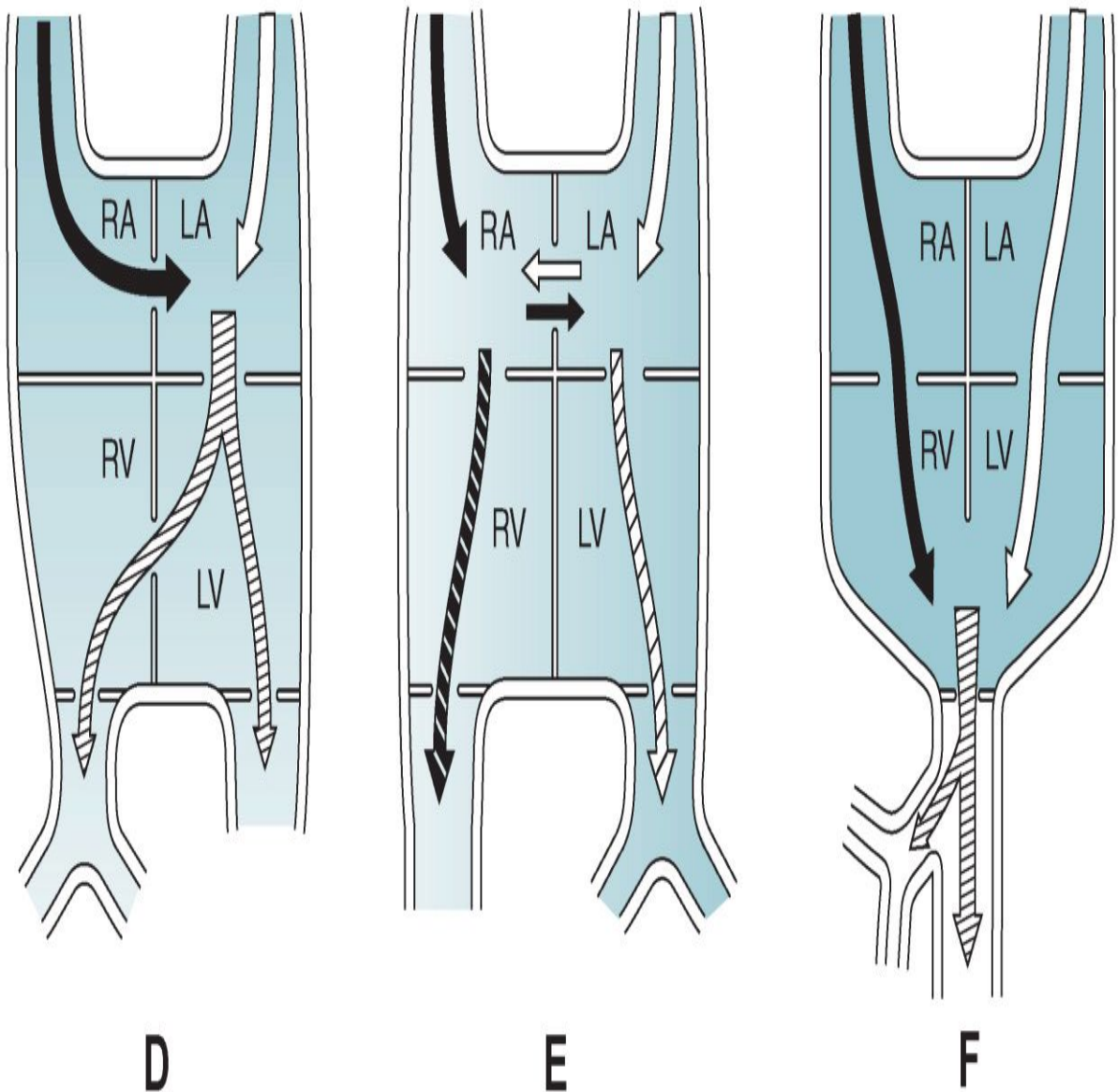
### *Considerations*

This boy has symptoms consistent with **cyanotic CHD** and likely has **TGA**. In this condition, the cardiac origins of the aorta and the pulmonary artery are switched, thus creating two parallel circuits of blood flow rather than the normal series circuit ([Figure 25-1](#)). This situation is **incompatible with life** unless a connection between the pulmonary and systemic circuits exists. During the first hours of life, the **ductus arteriosus and the foramen ovale**

**provide this connection;** symptoms develop when these connections begin to close. Some TGA patients also have a ventricular septal defect (VSD) and may first show signs of disease later in infancy. Management of the infant in this scenario consists of immediate steps to **maintain patency of the ductus arteriosus**.







**Figure 25-1.** Schematic drawing of circulation of various cardiac defects: (A) Normal circulation; (B) Tetralogy of Fallot; (C) Pulmonary artresia; (D) Tricuspid atresia; (E) Transposition of the great arteries; (F) Truncus arteriosus. Black arrows indicate deoxygenated blood; cross-hatched arrows indicate mixed blood; white arrows indicate oxygenated blood. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

APPROACH TO:



## Congenital Cyanotic Heart Disease

### DEFINITIONS

**CYANOSIS:** Bluish discoloration of the skin and mucous membranes caused by insufficient saturation of the blood with oxygen. Peripheral cyanosis is common in neonates and involves the extremities; it may be normal. Central cyanosis is always abnormal and is seen on the tongue, gingiva, and buccal mucosa.

**DUCTUS-DEPENDENT LESIONS:** Cardiac defects that are incompatible with life in the absence of a patent ductus arteriosus (PDA).

**RIGHT-TO-LEFT CARDIAC SHUNT:** Abnormal flow of blood across a cardiac defect from the right side of the heart containing deoxygenated blood to the left side of the heart where it is then pumped into the systemic circulation. These lesions result in cyanosis.

### CLINICAL APPROACH

**Cyanotic CHD often manifests itself after the PDA begins to close** (so the condition may be termed ductus dependent). Patency of the ductus maintains a connection between the pulmonary and systemic circulations; closure normally occurs on the first or second day of life in term infants. Previously, neonatal cyanotic CHD management involved emergency surgical repair on very sick infants; the introduction of **prostaglandin E<sub>1</sub>**, an **intravenously administered medication that keeps the ductus open**, now allows for infant stabilization prior to more definitive corrections.

**Cyanotic CHD is characterized by decreased pulmonary blood flow.** Unsaturated blood returning to the heart from the periphery is shunted into the systemic circulation, thus bypassing the lungs. This occurs whenever blood flow into the pulmonary system is compromised, as in pulmonary valve stenosis or if the origins of the pulmonary artery and aorta are switched (TGA).

**Pulse oximetry** can be used to measure the oxygen saturation of the tissues that are perfused by the portion of the aorta that is **proximal to the ductus (the right hand or an ear lobe)** and then is compared to tissues

perfused by the portion of the aorta that is **distal to the ductus (the lower extremity)**. If there is a **difference of more than 3% to 5%**, then there may be a **right-to-left shunt across the ductus**.

Transposition of the great arteries occurs in approximately 5% of children with congenital heart disease; it is the most common cardiac cause of cyanosis in neonates. **TGA typically causes an “egg-on-a-string” appearance on chest radiography** ([Table 25-1](#)), although the appearance may be normal in the first few days of life. Electrocardiography (ECG) shows the normal right ventricular hypertrophy seen in neonates. Diagnosis is confirmed with echocardiography.

Heart Anomaly	Radiographic Appearance
Tetralogy of Fallot	“Boot-shaped” heart and decreased pulmonary vascularity
Pulmonary atresia (with intact ventricular septum)	Decreased pulmonary vascularity
Tricuspid atresia (with normally related great vessels)	Decreased pulmonary vascularity
Epstein anomaly	Heart size may be normal to massive, with normal or decreased pulmonary vascularity
Transposition of the great arteries	“Egg-on-a-string” (narrow mediastinum) with normal to increased pulmonary vascularity
Truncus arteriosus	Cardiomegaly and increased pulmonary vascularity
Total anomalous pulmonary venous return	“Snowman” (supracardiac shadow caused by anomalous pulmonary veins entering the innominate vein and persistent left superior vena cava), and increased pulmonary vascularity
Hypoplastic left heart syndrome	Cardiomegaly and increased pulmonary vascularity

## **Table 25-1 • TYPICAL RADIOGRAPHIC FINDINGS OF COMMON HEART LESIONS**

**Initial management of TGA (after prostaglandins) involves creation of an atrial septum (“atrial septostomy”)** via cardiac catheterization, which provides immediate symptom palliation. Definitive surgical care often occurs in the first 2 weeks of life; postoperative stenosis at the repair sites is a potential long-term complication.

**Pulmonary valve stenosis**, another cyanotic CHD, accounts for approximately 7% of CHD. Cyanosis and exercise intolerance, if any, are proportional to the degree of stenosis. Examination reveals an upper left sternal border systolic murmur that radiates to the left infraclavicular area and a systolic click. The ECG is normal in mild cases, but greater degrees of stenosis cause right-axis deviation, right atrial hypertrophy, and right ventricular hypertrophy. Valvuloplasty is achieved through cardiac catheterization. Pulmonary stenosis may occur in conditions such as glycogen storage disease and Noonan syndrome.

**When pulmonary stenosis occurs with a large VSD, the result is known as tetralogy of Fallot (TOF).** With TOF, the intraventricular septum is displaced anteriorly, resulting in right ventricular outflow obstruction and displacement of the aorta over the right ventricle. Right ventricular hypertrophy develops as a result of the hemodynamic changes caused by the other abnormalities. The characteristic finding on chest radiograph is a **boot or wooden shoe appearance** (“coeur en sabot,” [Table 25-1](#)). If pulmonary stenosis is mild at birth, neonates have normal color (so-called pink tetralogy), but by early childhood most become cyanotic as a result of stenosis progression. **Many children with TOF also experience hypercyanotic spells (“tetralogy spells”)** caused by a sudden increase in right-to-left shunting of blood. These spells may be brought on by activity or agitation, or they may occur without an apparent precipitant. Such children can be seen assuming a squatting posture, which compresses peripheral blood vessels, thus increasing pulmonary blood flow and systemic arterial oxygen saturation. With current surgical management, 90% of patients with TOF survive to adulthood.

**Cyanosis is a hallmark of children who have tricuspid valve abnormalities of tricuspid atresia or Ebstein anomaly.** In tricuspid atresia, no outlet exists between the right atrium and the right ventricle, forcing

systemic venous return to enter the left atrium via the foramen ovale or an associated atrial septal defect; a VSD also is often present. The tricuspid valve of Ebstein anomaly is insufficient because two leaflets are displaced inferiorly into the right ventricle and unable to approximate each other; this also results in a smaller ventricle chamber and often obstructs ventricular outflow. Both conditions often are “ductal dependent” in the neonate, and both require surgical correction.

## COMPREHENSION QUESTIONS

- 25.1 A 12-year-old boy requires a sports physical examination. He denies chronic health problems, including adverse exertion symptoms. The clinician notes a I to II/VI left upper sternal border systolic murmur that does not radiate. The second heart sounds splits normally, and no audible click is appreciated. Peripheral perfusion is normal, and the fingers are not clubbed. Which of the following is the best recommendation?
- A. He should not play strenuous sports.
  - B. He can participate in sports without restrictions.
  - C. A chest radiograph and an ECG before further recommendation can be made.
  - D. A cardiology evaluation.
  - E. He may participate in sports, but he should seek immediate medical attention for dyspnea or other adverse symptoms.
- 25.2 A term, 3700-g infant is born vaginally without complications and has uneventful immediate neonatal course. At 2 weeks of age, a II/VI systolic murmur is noted in the mitral area that radiates to the back. A similar murmur is noted in the right axilla. The infant is pink and breathing easily, and the nurses notes show that he has been taking 30 cc of formula approximately every 2 hours. Initial management should include which of the following?
- A. Chest radiography, ECG, and four extremity blood pressures
  - B. Immediate administration of prostaglandin E<sub>1</sub>
  - C. Admission to the pediatric intensive care unit
  - D. Consultation by a pediatric cardiologist

E. Close follow-up in your pediatric clinic

**25.3** A 4-year-old boy presents for a well-child visit. His mother notes that he breathes fast and his lips turn “dusky” when he runs or plays hard. The symptoms resolve once he stops the activity. On examination, he has a II/VI left upper sternal border systolic murmur that radiates to the back; a faint click is heard. Which of the following is the most likely cause of this child’s exercise intolerance?

A. Asthma

B. Atrial septal defect

C. Pulmonary valve stenosis

D. Tricuspid atresia

E. Ventricular septal defect

**25.4** A 15-month-old girl is playing quietly in your waiting room. The skin around her mouth is faintly blue, but she appears comfortable. She arises from her squatting position to run after her brother, and she suddenly becomes dyspneic and cyanotic. She returns to a squatting position and soon is breathing comfortably with only slight perioral cyanosis. Which of the following would you expect to see on her chest radiograph?

A. A “boot-shaped” heart

B. An “egg on a string”

C. Lung hyperinflation

D. Pneumonia

E. Pulmonary congestion

## ANSWERS

**25.1 B.** This child has a benign pulmonary flow murmur, differentiated from a pathologic pulmonary murmur in that it does not radiate, no click is heard, and no signs and symptoms of cardiac disease (digital clubbing, cyanosis, exercise intolerance) are found.

**25.2 E.** This infant has peripheral pulmonic stenosis, a benign childhood murmur. Other frequently encountered benign childhood murmurs are the venous hum (a low-pitched murmur heard at the sternal notch only when

the child is upright) and the Still vibratory murmur (a high-pitched “musical” systolic murmur heard best at the left sternal border in the supine position). Although it may be difficult to diagnose the multitude of pathologic heart sounds, clinicians certainly should know the characteristics of the common benign childhood murmurs.

- 25.3 C. Although pulmonary stenosis and tricuspid atresia are cyanotic heart lesions, exercise-induced cyanosis and systolic murmur are characteristic of pulmonary stenosis.
- 25.4 A. This child has TOF; she experiences improvement when squatting and “tet” (hypercyanotic) spells when running. The “boot-shaped” heart is a characteristic chest radiographic finding.
- 

### CLINICAL PEARLS

- Cyanotic congenital heart disease is characterized by decreased pulmonary blood flow (right-to-left shunt). Transposition of the great arteries and defects of the tricuspid valve and pulmonary outflow tract are examples of cyanotic heart defects.
  - Lesions of congenital heart disease incompatible with life except in the presence of a PDA are termed “ductus dependent.”
  - Prostaglandin E<sub>1</sub> is often used in infants with cyanotic congenital heart disease to maintain the patent ductus arteriosus until more definitive surgical correction can be attempted.
  - The heart defects in tetralogy of Fallot are: (1) ventricular septal defect, (2) pulmonic stenosis, (3) overriding aorta, and (4) right ventricular hypertrophy.
- 

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## CASE 26

A 3-year-old boy has a 20-day history of high fevers that spike twice daily. He was diagnosed with otitis media on the fifth day of fever and was prescribed amoxicillin, but the fever persisted. The fever is associated with a faint rash on the trunk and proximal extremities and complaints of "body aches." A chest radiograph is normal, but a complete blood count (CBC) shows a hemoglobin of 9.8 mg/dL, a hematocrit of 29.9%, a white blood cell count of  $18,000/\text{mm}^3$ , and a platelet count of  $857,000/\text{mm}^3$ . He has developed an aversion to bearing weight and continues to have fevers to  $102.5^{\circ}\text{F}$  ( $39.2^{\circ}\text{C}$ ), but otherwise he has normal vital signs. His examination is remarkable for scattered lymphadenopathy, hepatosplenomegaly, and mild swelling of his interphalangeal joints and knees.



- ▶ What is the most likely diagnosis?
- ▶ What is the best diagnostic test for this disorder?
- ▶ What is the treatment for this condition?

## ANSWERS TO CASE 26: **Juvenile Idiopathic Arthritis (JIA)**

*Summary:* A 3-year-old boy has 20 days of high-spiking fevers and a rash and “body aches” that wax and wane with the fevers. He also has a 1-day history of refusal to bear weight. His examination is significant for lymphadenopathy, organomegaly, and joint swelling. His chest radiograph is negative, but the CBC reveals leukocytosis, thrombocytosis, and anemia.

- **Most likely diagnosis:** Systemic-onset juvenile idiopathic arthritis (JIA; previously termed juvenile rheumatoid arthritis).
- **Best diagnostic test:** No laboratory studies are diagnostic for JIA, but a history plus a CBC, blood cultures, erythrocyte sedimentation rate (ESR), rheumatoid factor (RF), antinuclear antibody (ANA), and synovial fluid assessment can aid in establishing or eliminating this diagnosis.
- **Treatment:** Nonsteroidal anti-inflammatory drugs (NSAIDs), methotrexate, and glucocorticoids can be used to control symptoms. Physical and occupational therapy are important for preserving function and preventing deformity.

## ANALYSIS

### *Objectives*

1. Know the three forms of JIA and their most common presenting signs and symptoms.
2. Recognize systemic-onset JIA as an important consideration in the evaluation of childhood fever of unknown origin (FUO).

### *Considerations*

The **differential diagnosis for childhood FUO** is long and includes **infectious, hematologic, and rheumatologic causes**. The fever pattern can

sometimes aid in narrowing the diagnostic possibilities. In this case, the **daily high-spiking fevers associated with a characteristic rash are suggestive of systemic JIA**. Organomegaly and lymphadenopathy also are characteristic of systemic JIA. Arthritis may develop after other symptoms begin, as in this case, sometimes appearing months or even years into the disease course. For cases where arthritis first appears late in the disease course, leukemia may be a consideration.

APPROACH TO:

**Juvenile Idiopathic Arthritis**

## DEFINITIONS

**ARTHRALGIA:** Any pain that affects a joint.

**ARTHRITIS:** Swelling or effusion of a joint, or the presence of two or more of the following signs: limited range of motion, tenderness or pain on motion, and increased heat in one or more joints.

**SYSTEMIC-ONSET JIA:** Characterized by arthritis with fever, evanescent rash, hepatosplenomegaly, serositis, and lymphadenopathy.

**OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS (OLIGOARTHRITIS):** JIA with involvement of one to four joints.

**POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS (POLYARTHRITIS):** JIA with involvement of five or more joints.

## CLINICAL APPROACH

**Juvenile idiopathic arthritis is the most common rheumatologic disorder in children.** The diagnosis specifies onset prior to the age of 16 years and symptom duration of 6 weeks or longer. Other causes of arthritis in children (infectious and other rheumatologic causes) must be excluded; in the **sexually active adolescent, gonococcal arthritis must be considered.** Three diverse entities fall under the JIA rubric, classified according to symptoms occurring in the first 6 months of illness: **(1) systemic-onset disease, (2) polyarticular disease, and (3) oligoarticular disease.**

Systemic symptoms dominate the clinical scene in systemic-onset JIA, making the diagnosis difficult if frank arthritis is not present. **Daily high-spiking fevers for 2 weeks or more, a rash and arthralgias that wax and wane with the fever, lymphadenopathy, and organomegaly are characteristic of systemic-onset disease.** Pericarditis, hepatitis, pleural effusion, and encephalopathy also may occur.

**Polyarticular disease** is diagnosed when **five or more joints are involved** and systemic signs and symptoms are mild or absent. This disease is more common in girls and has a biphasic age of onset (most cases occur at ages 1 to 3 years and the remainder occur at ages 9 to 12 years). The younger patients are usually RF negative, while the older age group is often RF positive. The presence of this factor tends to cause a disease presentation similar to adult rheumatoid arthritis. The **cervical spine, temporomandibular joints, shoulders, and hips** are the most commonly affected joints.

**Oligoarticular JIA** is the most common form and involves fewer than five joints. It is divided into persistent and extended categories; extended refers to the disease progressing to affect more than four joints after the first 6 months. Oligoarthritis occurs predominantly in toddler-aged females, and serum ANA often is positive. The **knee** is most commonly affected, followed by the **ankle**. It is crucial for these children to have frequent **ophthalmologic screenings** as one-fourth of them will develop asymptomatic iridocyclitis (iris and ciliary body inflammation; also called “anterior uveitis”). Eye disease does not parallel the arthritis activity.

The initial laboratory evaluation for the child with suspected systemic JIA includes a CBC, ESR, and blood cultures. **Leukocytosis, thrombocytosis, and anemia support the diagnosis of systemic JIA.** The ESR is elevated, and blood cultures are negative. **Evaluation of synovial fluid** may be necessary to rule out septic arthritis, particularly in the presence of exquisitely tender joints or when only a single joint is involved. Rheumatoid factor and ANA usually are negative in systemic JIA.

**Medications** for JIA include **NSAIDs, steroids, methotrexate**, and other immunosuppressive agents. Physical and occupational therapy are vital for maintaining joint function and preventing further deformities. **Routine slit-lamp ophthalmic examinations to monitor for uveitis** are indicated. Approximately 50% of children will have their JIA persist into adulthood.

## COMPREHENSION QUESTIONS

- 26.1 A 14-year-old girl has a 1-week history of arthritis involving her hands, wrists, knees, and ankles. At the onset she had noted that her cheeks seemed flushed; this resolved and has been followed by a slightly pruritic red macular rash over her torso and proximal extremities that is

now clearing in some areas. On review of systems, she reports rhinorrhea and a low-grade fever 2 weeks ago. On examination, she has tender swelling of the aforementioned joints and an erythematous macular rash with a reticular pattern. Which of the following findings would help identify the most likely diagnosis?

- A. Positive rheumatoid factor
- B. Reticulocyte count of 0%
- C. Anemia
- D. Skin biopsy of the rash
- E. Synovial fluid analysis

26.2 A 5-year-old girl is referred to a pediatric rheumatologist with a 4-week history of mild swelling and decreased range of motion in the left knee and right elbow. She is afebrile and appears otherwise well. Positive findings on which of the following evaluations will be most helpful in establishing her diagnosis?

- A. Arthrocentesis
- B. Complete blood count
- C. Computerized tomographic scan of the involved joints
- D. Slit-lamp examination of her eyes
- E. Bone scan

26.3 A 6-year-old boy presents with his mother after developing acute right groin and knee pain that causes him to limp. He and the mother do not recall any trauma. Review of systems is positive only for rhinorrhea and sore throat 2 weeks ago. On examination, he is afebrile and his knee exam is normal, but he walks with a right toe-touch gait. Which of the following are the most appropriate next steps in his evaluation?

- A. Assess range of motion of the right hip; measure WBC and ESR; perform ultrasound of the right hip.
- B. Perform ophthalmologic exam; measure ANA and RF; perform x-ray of the knee.
- C. Perform a full skin exam; interview the child alone about abuse; perform a skeletal survey.

- D. Ask the mother about bleeding disorders; measure coagulation factors; perform aspiration of the knee.
  - E. Interview the child and mother about recent school stressors; provide reassurance to the mother that he is exaggerating growing pains for secondary gain; refer to counseling services.
- 26.4 A 3-year-old boy with suspected systemic-onset JIA develops tachycardia and dyspnea on the fifth hospital day. He complains that his chest hurts. Heart auscultation reveals a “friction rub” sound. Which of the following is the next best step in management?
- A. Give him a nebulized albuterol treatment.
  - B. Give him a dose of furosemide.
  - C. Give him some acetaminophen.
  - D. Check his oxygenation status through pulse oximetry, obtain a stat electrocardiogram, and consult with a pediatric cardiologist.
  - E. Check his oxygenation status via pulse oximetry, obtain a stat chest x-ray, and initiate intravenous antibiotics.

## ANSWERS

- 26.1 **B.** The differential diagnosis for childhood arthritis includes infectious and rheumatologic disorders. Her symptoms and physical examination findings are typical of *parvovirus B19* infection. Patients with this infection can have a transiently positive RF and often will have mild anemia. Parvovirus B19 targets erythroid precursors; there is no compensatory reticulocytosis as these are lysed by the virus. The other studies would not be helpful in distinguishing the etiology of the arthritis.
- 26.2 **D.** JIA is the most common cause of uveitis in children. Uveitis onset may be insidious, and may be the only initial manifestation of JIA. The disease is more common in young girls. Slit-lamp findings include band keratopathy, posterior synechiae, and cataracts. Children with JIA should have periodic slit-lamp examinations in order to detect eye disease early. Consideration may be given to obtaining the tests suggested in the other answer choices, but positive results on these tests are unlikely to be specific for JIA.

- 26.3 A. A good rule of thumb is to examine one joint above and one joint below the site of symptoms. Hip pain may refer to the groin, anterior thigh, or knee. If the hip's range of motion is near-normal, WBC and ESR are normal, and ultrasound shows a joint effusion, the most likely diagnosis is transient (toxic) synovitis of the hip.
- 26.4 D. A friction rub is characteristic of pericarditis, which is a common and serious complication of systemic-onset JIA. The friction rub is a “grating” or “creaking” sound that often is best heard along the left sternal border. Patients typically complain of chest pain that is relieved when the patient is asked to lean forward, and worsened by deep inspiration or coughing; however, pain is not always present. Rarely, pericarditis in JIA may precede the development of arthritis by months or even years. Low-voltage QRS complexes and ST-segment elevation may be seen on the electrocardiogram. Treatment consists of salicylates or steroids.
- 

### CLINICAL PEARLS

- The spectrum of juvenile idiopathic arthritis comprises three entities: (1) systemic-onset disease, (2) polyarticular disease, and (3) oligoarticular disease.
  - Systemic-onset juvenile idiopathic arthritis is an important consideration in the differential diagnosis of childhood fever of unknown origin.
  - The diagnosis of juvenile idiopathic arthritis is based on clinical criteria and by the exclusion of other possibilities; no single laboratory test confirms the diagnosis.
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## CASE 27

A 2-year-old girl, born at 32 weeks' gestation, comes to your clinic for an initial visit. Her 1-month stay in the neonatal intensive care unit was complicated by necrotizing enterocolitis (NEC), requiring surgical removal of a small section of her intestine that included the ileocecal valve. She had an uncomplicated postoperative course, and her mother declares she has been developing normally and gaining weight. She has a healthy appetite, a varied diet, and no history of abnormal stooling. Her mother is concerned, though, that she has been getting progressively paler since her last clinic visit with another provider 6 months ago. Physical examination reveals an overall healthy-appearing toddler with normal vital signs. She has pallorous skin and conjunctivae and a well-healed abdominal surgical scar. The remainder of her physical examination is normal. You order a complete blood count (CBC) and a reticulocyte count and find that the hemoglobin is 7 g/dL, the mean corpuscular volume is 110 fL, and the reticulocyte count is 2%.

- What is the most likely cause of this child's anemia?
- How should she be treated?

ANSWERS TO CASE 27:



## Macrocytic (Megaloblastic) Anemia Secondary to Vitamin B<sub>12</sub> Deficiency

*Summary:* A 2-year-old former premature infant with history of NEC and intestinal resection presenting with pallor and anemia.

- **Most likely cause:** Vitamin B<sub>12</sub> deficiency secondary to terminal ileal resection and compromised intestinal absorption.
- **Treatment:** Monthly intramuscular vitamin B<sub>12</sub> supplementation.

## ANALYSIS

### *Objectives*

1. Describe the typical findings in macrocytic anemia.
2. List the potential causes of macrocytic anemia.
3. Understand the treatment options for macrocytic anemia.

### *Considerations*

Evaluation of a child with suspected anemia involves performing thorough personal and family histories and a comprehensive physical examination. Anemia can result from a variety of disorders, including defective red blood cell production, hemolysis, or blood loss. The clinician's goal, therefore, is to gather historical clues (atypical patient or family dietary histories, family history of blood dyscrasias) and examination findings (splenomegaly, flow murmur, hematochezia) that are important in guiding appropriate diagnostic and therapeutic plans.

APPROACH TO:

**Macrocytic Anemia**

## DEFINITIONS

**MEAN CORPUSCULAR VOLUME (MCV):** Average size of a red blood cell; large cells are macrocytic; small cells are microcytic.

**RETICULOCYTE COUNT:** Percentage of red blood cells that are immature (new).

**INTRINSIC FACTOR:** Glycoprotein secreted in the stomach that binds to vitamin B<sub>12</sub>; the intrinsic factor–vitamin B<sub>12</sub> complex then attaches to receptors in the distal ileum and is absorbed.

## CLINICAL APPROACH

**Anemia typically is distinguished by the size of the red blood cells. Children with iron deficiency develop a microcytic anemia and typically have a low MCV;** their red blood cells are smaller than normal because of the decreased amount of hemoglobin in each cell. Children who quickly lose a large amount of blood usually have a normocytic anemia; the cells are normal, but there are fewer of them.

Various conditions may result in **macrocytic anemia, usually associated with an elevated MCV. Hypothyroidism, trisomy 21, vitamin B<sub>12</sub> deficiency,** and folate deficiency often are associated with macrocytic anemia and a low reticulocyte count, as a result of inadequate bone marrow production. A macrocytic anemia also may be seen with active hemolysis, but usually this anemia is accompanied by an elevated reticulocyte count.

Vitamin B<sub>12</sub>-mediated macrocytic anemia can occur as a result of dietary deficiency, malabsorption, or inborn errors of metabolism. Vitamin B<sub>12</sub>, an important factor in DNA synthesis, is available in many foods (meats, fish, eggs). A pure dietary deficiency is rare in children, but diets devoid of all animal products may result in a deficiency. **Breast-fed infants of mothers who adhere to a strict vegan diet are at risk for vitamin B<sub>12</sub> deficiency.** Malabsorption can occur when the terminal ileum is absent, as in this case scenario, or when infectious or inflammatory conditions compromise intestinal function.

Children with the rare condition “juvenile pernicious anemia” are unable to secrete intrinsic factor and become vitamin B<sub>12</sub> deficient between the ages of 1 and 2 years, when the supply of vitamin B<sub>12</sub> passed transplacentally from mother to child is exhausted. These children will exhibit worsening irritability, loss of appetite, and decreased activity. Children affected with this condition are at risk for permanent neurologic damage resulting from spinal cord demyelination. Therapy is intramuscular vitamin B<sub>12</sub> replacement. High-dose oral replacement may be corrective (limited,

inconclusive studies at present) in patients with intrinsic factor deficiency or severe dietary deficiency that cannot be corrected with dietary modification.

A variety of other more unusual causes of vitamin B<sub>12</sub> deficiency can be listed. The fish tapeworm *Diphyllobothrium latum* uses vitamin B<sub>12</sub>, and intestinal infestation can result in macrocytic anemia. Similarly, any intestinal infectious or inflammatory process, such as parasitic infection or inflammatory bowel disease, could promote vitamin B<sub>12</sub> deficiency. Infants exclusively fed on goat's milk, nutritionally deficient in both vitamin B<sub>12</sub> and folate, are at risk not only for vitamin B<sub>12</sub> deficiency but also brucellosis if the milk is unpasteurized. For infants fed on goat's milk, vitamin and mineral supplementation is required.

Treatment for B<sub>12</sub> deficiency is guided by the underlying disorder. Eradicating or suppressing a gastrointestinal infection or inflammatory disorder should promote sufficient mucosal repair to permit adequate vitamin B<sub>12</sub> absorption, and further vitamin B<sub>12</sub> therapy may not be required. For patients with an inability to produce intrinsic factor and for those with absence or permanent dysfunction of the gastric antrum or terminal ileum (the site of intrinsic factor production and absorption, respectively) monthly parenteral vitamin B<sub>12</sub> therapy is indicated.

For patients with macrocytosis but normal B<sub>12</sub> and folate levels, consideration for atypical bone marrow pathology (such as leukemia or myelodysplasia) must be entertained. Referral to a pediatric hematologist would be warranted.

## COMPREHENSION QUESTIONS

- 27.1 You are called to the bedside of a mother who just delivered a healthy term infant and has a question regarding her infant's nutrition. The mother was fed goat's milk as a child and wants to do the same for her infant. Under which of the following conditions is goat's milk acceptable as infant nutrition?
- A. Goat's milk proteins are hydrolyzed before feeds.
  - B. Infants are provided supplemental vitamins and minerals.
  - C. Goat's milk is freshly obtained from goats.

D. Infants of mothers with milk intolerance should preferentially receive goat's milk.

E. Goat's milk is diluted with water.

27.2 You receive the results of a CBC you performed in your clinic on a pallorous 9-month-old boy. Other than pallor, no historical or physical examination concerns were noted during the patient's visit. The laboratory technician reports a hemoglobin of 8.6 g/dL, an MCV of 105 fL, and platelet count of 98,000/mm<sup>3</sup>. You are also told that the white blood cell count is 8500/mm<sup>3</sup> and the differential reveals 47% neutrophils and 42% lymphocytes, and that no atypical lymphocytes are seen. Which of the following is the most appropriate next step in this child's care?

A. Measure serum iron and total iron binding capacity levels.

B. Begin oral iron supplementation.

C. Measure vitamin B<sub>12</sub> and folate levels.

D. Begin oral vitamin B<sub>12</sub> and folate supplementation.

E. Obtain a stat referral to pediatric hematologist.

27.3 The parents of a previously healthy 3-year-old girl bring the child to your clinic because she is complaining that her tongue hurts. The parents also report that she has appeared weak and listless over the last several months, and has not been eating well. Recently she has exhibited trouble walking. The family usually eats a regular diet, including meats and vegetables. On physical examination, she is pale and tachycardic. Her complete blood count reveals a macrocytic anemia. You suspect a vitamin or mineral deficiency. What additional finding is most likely in this toddler?

A. Red tongue

B. Petechiae and ecchymoses

C. Muscle fasciculation

D. Hair loss

E. Blue sclerae

- 27.4 You are working at a Native American clinic in Alaska. A 16-year-old adolescent female comes to your clinic for an evaluation of lethargy. Her father notes that recently she has looked pale. She eats a regular diet and has no significant past medical history. Her menses are regular and have not been excessive. During the last few years, she has helped her mother in the family seafood restaurant after school, but is increasingly tired and unable to complete all of her work. Her CBC reveals a megaloblastic anemia. Which of the following is the next appropriate study?
- A. Folate level
  - B. Stool for rotavirus
  - C. Iron level
  - D. Stool for ova and parasites
  - E. Transcobalamin level

## ANSWERS

- 27.1 **B.** Infants drinking goat's milk must have nutritional supplementation with vitamin B<sub>12</sub>, folate, and iron. Several goat's milk-based formulas including these nutrients are available. Fresh, unpasteurized goat's milk can contain *Brucella ovis* and cause brucellosis. Diluting milk will only serve to dilute the caloric content.
- 27.2 **C.** This infant has hematologic parameters consistent with macrocytic anemia. The mild thrombocytopenia reported is periodically seen in patients with vitamin B<sub>12</sub> deficiency, and is thought to be related to impaired DNA synthesis and ineffective thrombopoiesis. The results reported are not typical for iron deficiency, and neither an iron panel nor iron supplementation is warranted. At this point, your workup should include checking folate and B<sub>12</sub> levels; supplementation of these compounds is not yet justified. Myelodysplasia or leukemia is in the differential, but is probably less likely with a normal white blood cell count and differential (no atypical cells); referral to pediatric hematology may ultimately be required, but some preliminary data can be gathered first.

- 27.3 **A.** A smooth, red, and tender tongue may be observed in juvenile pernicious anemia, a rare autosomal recessive condition in which the child is not able to secrete intrinsic factor and cannot absorb vitamin B<sub>12</sub>. Supplies of vitamin B<sub>12</sub> passed to the fetus from the mother typically are sufficient for at least the first 1 to 2 years of life. A deficiency in transcobalamin results in megaloblastic anemia in infancy because transcobalamin is required for B<sub>12</sub> transport and utilization; therefore, vitamin B<sub>12</sub> provided by the mother cannot be used effectively. Petechiae may occur with vitamin C or K deficiency, muscle fasciculation with vitamin D and calcium disturbance, and hair loss with zinc deficiency.
- 27.4 **D.** The fish tapeworm *Diphyllobothrium latum* uses vitamin B<sub>12</sub> for growth and egg production; as many as one million eggs per day may be produced. The parasite also inactivates the vitamin B<sub>12</sub>–intrinsic factor complex, inhibiting absorption in the terminal ileum. The fish tapeworm is the longest tapeworm to infect humans, sometimes growing to more than 10 m in length. Most infestations are asymptomatic, with megaloblastic anemia occurring in 2% to 9% of tapeworm infections. Risk factors include eating raw or undercooked fish. In North America, it is most commonly seen in the northern United States, Alaska, and Canada. Eggs have a unique morphology and are easily found in stool samples.
- 

### CLINICAL PEARLS

- Vitamin B<sub>12</sub> dietary deficiency is rare; infants breast-fed by vegan mothers are at risk to become vitamin B<sub>12</sub> deficient and should receive supplementation.
  - Infants drinking goat's milk must be supplemented with vitamin B<sub>12</sub>, folate, and iron.
  - Vitamin B<sub>12</sub> deficiency related to gastric antrum or ileal resection requires parenteral vitamin B<sub>12</sub> supplementation.
  - Vitamin B<sub>12</sub> deficiency can lead to permanent neurologic damage.
- 

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## CASE 28

A 3-year-old boy arrives to the emergency department after having suffered a seizure. The family reports that they had moved to Baltimore from the Midwest 3 months ago. The child was the product of a normal pregnancy and delivery, and he had experienced no medical problems until the move. The parents report that he has developed emotional lability, abdominal pain, “achy bones,” and intermittent vomiting and constipation. They initially attributed his behavior to the move and to the chaos in their house, which is being extensively renovated.

- What is the most likely diagnosis?
- What is the best test to diagnose this condition?
- What is the best therapy?

## ANSWERS TO CASE 28: **Lead Toxicity**

*Summary:* A 3-year-old, previously healthy child now living in a home undergoing extensive renovation has developed seizures, neurologic changes, and abdominal complaints.

- **Most likely diagnosis:** Lead toxicity.
- **Best test:** Blood lead level (BLL).
- **Best therapy:** Remove child from lead source and initiate chelation therapy.

## ANALYSIS

### *Objectives*

1. Understand the signs, symptoms, and treatment of lead poisoning.
2. Be familiar with the environmental sources of lead.
3. Understand the sources of other environmental exposures.

### *Considerations*

This child is demonstrating signs and symptoms of lead poisoning. He may have been exposed to dust in the environment, or he may have displayed pica (the eating of nonfood substances such as paint chips, dirt, or clay). Therapy can be initiated immediately while awaiting the blood lead level. During the evaluation and treatment, other children in the home must be screened for elevated lead levels as well.

*Note:* Lead exposure sources vary across the United States. In the northeastern United States, older homes undergoing renovation are common sources of exposure. Leaded paint is far less common in other parts of the country. A complete investigation includes a travel history and an accounting of lead exposures through hobbies (such as stained glass), home renovation, welding, radiator repair, furniture refinishing, and similar activities.

### APPROACH TO:

#### **Lead Poisoning**

## DEFINITIONS

**CHELATING AGENT:** A soluble compound that binds a metal ion (in this case lead) so that the new complex is excreted in the urine.

**PLUMBISM:** Alternate name for lead poisoning.



## CLINICAL APPROACH

The incidence of lead poisoning in the United States has decreased dramatically over the last 20 years. Previous sources (gasoline, foods, beverage cans) have been eliminated; **lead-containing paint in older homes is now the major source.** Less common sources include foodstuffs from countries where regulations are not strict, **glazed pottery, ingestion of leaded items (jewelry, fishing equipment), and exposure through burning of lead-containing batteries or through hobbies involving lead smelting.** Several lines of toys were recalled by the US Consumer Product Safety Commission in 2010 when they were found to be coated with lead-based paint.

The signs and symptoms vary from none (especially at lower lead levels) to those listed in this case. However, symptoms may be seen at low blood lead levels (BLLs), and a child with very high BLLs occasionally may be asymptomatic. **Anorexia, hyperirritability, altered sleep pattern, and decreased play are commonly seen. Developmental regression, especially with speech, may also be present.** Abdominal complaints (occasional vomiting, intermittent pain, and constipation) are sometimes noted. **Persistent vomiting, ataxia, altered consciousness, coma, and seizures are signs of encephalopathy.** Permanent, long-term consequences include learning and cognitive deficits and aggressive behavior; with less lead in the environment and decreasing average lead levels, these more subtle findings are now more common than acute lead encephalopathy.

The BLL is the diagnostic test of choice, and demonstrates recent ingestion; however, a significant amount of lead is stored in other tissue, most notably bone. BLL, then, does not accurately reflect total body lead load. Other tests (free erythrocyte protoporphyrin, basophilic stippling, glycosuria, hypophosphatemia, long bone “lead lines,” and gastrointestinal tract radiopaque flecks) in symptomatic patients are less specific.

**Treatment varies depending on the BLL and the patient’s symptoms. Admission to the hospital, stabilization, and chelation are appropriate for symptomatic patients.** Therapy for asymptomatic patients could involve simple investigation of the child’s environment, outpatient chelation, or immediate hospitalization ([Table 28-1](#)). Close contact with local health

agencies is important; they usually are charged with ensuring that the child's environment is lead-free.

Blood Lead Level ( $\mu$ g/dL)				
10-14	15-19	20-44	45-69	$\geq 70$
Lead education • Dietary • Environmental Follow-up blood lead monitoring	Lead education • Dietary • Environmental Follow-up blood lead monitoring Proceed according to actions for 20-44 $\mu$ g/dL if: • A follow-up BLL is in this range at least 3 months after initial venous test Or • BLLs increase	Lead education • Dietary • Environmental Follow-up blood lead monitoring Complete history and physical exam Lab work: • Hemoglobin or hematocrit • Iron status Environmental investigation Lead hazard reduction Neurodevelopmental monitoring	Lead education • Dietary • Environmental Follow-up blood lead monitoring Complete history and physical exam Complete neurological exam Lab work: • Hemoglobin or hematocrit • Iron status • Free erythrocyte protoporphyrin (FPP) or zinc protoporphyrin	Hospitalize and commence chelation therapy Proceed according to actions for 45-69 $\mu$ g/dL

	Abdominal x-ray (if particulate lead ingestion is suspected) with bowel decontamination if indicated	(ZPP) Environmental investigation Lead hazard reduction Neurodevelopmental monitoring Abdominal x-ray with bowel decontamination if indicated Chelation therapy	
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*The following actions are NOT recommended at any blood lead level:*

- Searching for gingival lead lines
- Testing of hair, teeth, or fingernails for lead
- Testing of neurophysiologic function
- Radiographic imaging of long bones
- Evaluation of renal function (except during chelation with EDTA)
- X-ray fluorescence of long bones

*Reproduced from the Centers for Disease Control and Prevention, [www.cdc.gov](http://www.cdc.gov).*

### Table 28-1 • SUMMARY OF RECOMMENDATIONS FOR CHILDREN WITH CONFIRMED (VENOUS) ELEVATED BLOOD LEAD LEVELS

**Chelation** in an asymptomatic child may consist of intramuscular calcium disodium ethylenediaminetetraacetic acid (CaEDTA) or more commonly oral meso-2,3-dimercaptosuccinic acid (DMSA, succimer). Hospitalized symptomatic patients are often treated with 2,3-dimercaptopropanol (British anti-Lewisite [BAL]) and CaEDTA. Fluid balance is tricky; urine output is maintained because CaEDTA is renally excreted, but encephalopathy may be exacerbated with overhydration.

Newer research has cast doubt on the utility of chelation therapy in children with lead levels less than 45 µg/dL. Lead levels do decrease acutely with chelation therapy, but affected children do not show improvement in long-term cognitive testing. In fact, the most recent literature suggests that

there is no “safe” lead level; even lead levels less than 10 µg/dL have been shown to have a deleterious impact on neurocognitive development. This evidence places further importance upon the primary prevention of lead exposure in children.

Targeted BLL screening of at-risk children rather than universal screening is recommended. Questionnaires to assess the risk of lead exposure query the age of the home or day care center, the possibility of exposure to high-lead environments (battery recycling plant, lead smelter, etc), or environments in which others (siblings, playmates, etc) with elevated BLLs have been identified. Some state and federal programs, such as Early Periodic Screening, Diagnosis, and Treatment (EPSDT) and Healthy Kids, provide further guidance on lead screening.

## COMPREHENSION QUESTIONS

- 28.1 A developmentally normal 2-year-old child is in your inner city clinic for a well-child check. As part of the visit, you obtain a blood lead level and a hemoglobin level in accordance with your state’s Medicaid screening guidelines. The following week, the state lab calls your clinic to report that the child’s blood lead level is 14 µg/dL. Appropriate management of this level should include which of the following actions?
- A. Initiate chelation therapy.
  - B. Perform long bone radiographs.
  - C. Reassure the parents that no action is required.
  - D. Repeat the blood lead level in 3 months.
  - E. Report to the local health department for environmental investigation.
- 28.2 While evaluating the family in the previous question, you discovered a 3-year-old sibling with a lead level of 50 µg/dL. You reported the case to the local authorities and initiated chelation therapy. All lead sources in the home have since been removed (verified by dust wipe samples), and the parents do not work in occupations prone to lead exposure. After a course of outpatient chelation therapy, the 3-year-old’s lead level dropped to 5 µg/dL. Today, however, the child’s 3-month follow-up blood lead level is 15 µg/dL. At this point, appropriate management includes which of the following actions?

- A. Initiate a course of inpatient parenteral chelation therapy.
- B. Perform long bone radiographs.
- C. Reassure the parents and repeat a blood lead level in 3 months.
- D. Recommend the family move to another home.
- E. Repeat a course of outpatient chelation therapy.

28.3 A term newborn infant is admitted to the Neonatal ICU after having a seizure in the Well Baby Nursery. Your examination reveals a microcephalic infant with low birth weight who does not respond to sound. In your discussions with the family, you discover this is the parents' first child. They recount odd symptoms that have developed in the both of them in the last few months, including fine tremors in their upper extremities and blurry vision. They also note that they both can no longer smell their food and that it "tastes funny." The mother notes that she has had trouble walking straight in the last few weeks, but she attributes that to her pregnancy. Which of the following environmental toxins is most likely to have caused these findings?

- A. Inorganic arsenic salts
- B. Lead
- C. Methyl mercury
- D. Orellanine
- E. Polychlorinated biphenyls

28.4 A previously healthy 2-year-old boy is brought to the emergency department by ambulance after having a generalized tonic-clonic seizure at home. The mother reports that she put him to bed early the night before because she was having some friends over for a Bunco party. This afternoon when she awoke she found him wandering around the house, seemingly off balance, and he was "not acting right." She called EMS as soon as he had his seizure. The responding paramedic reported that the child's initial blood glucose was 15 mg/dL; after administration of lorazepam and a bolus of D10W he stopped seizing. Upon examination you find a heart rate of 110 beats/min, a respiratory rate of 20 breaths/min, a temperature of 37°C (98.6°F), and a blood pressure of 89/43 mm Hg. His pupils are reactive, and his funduscopic examination

is normal. The rest of his examination is benign. Which of the following is the most likely cause of the seizure?

- A. 3,4-Methylenedioxymethamphetamine (MDMA; “Ecstasy”) ingestion
- B. Brain tumor
- C. Ethanol ingestion
- D. Exogenous insulin administration
- E. Head trauma

## ANSWERS

- 28.1 D.** The patient’s lead screen is mildly elevated. Appropriate management includes educating the parents about potential lead exposures in the environment as well as in the diet. A repeat level should be performed in 3 months. Chelation therapy is currently advised for patients with a blood lead level of 45 µg/dL and above. Environmental investigation is recommended in patients with a blood lead level of 20 µg/dL and above, or if levels remain elevated despite educational efforts. Long bone radiographs are not recommended at any blood lead level.
- 28.2 C.** In this case, reassurance is appropriate. Lead deposits in bone, and chelation does not remove all lead from the body. After chelation is complete, lead levels tend to rise again; the source is thought to be the redistribution of lead stored in bone. Repeat chelation is only recommended if the blood lead level rebounds to 45 µg/dL or higher. Moving to another home is not necessary, assuming the health department successfully remediated their current home. Long bone radiographs are not recommended at any blood lead level.
- 28.3 C.** Infants exposed in utero to methyl mercury may display low birth weight, microcephaly, and seizures. They also display significant developmental delay and can have vision and hearing impairments. Symptoms in children and adults include ataxia, tremor, dysarthria, memory loss, altered sensorium (including vision, hearing, smell, and taste), dementia, and ultimately death. Acute ingestion of arsenic causes severe gastrointestinal symptoms; chronic exposure causes skin lesions and can cause peripheral neuropathy and encephalopathy. Orellanine is a toxin found in the *Cortinarius* species of mushroom that causes nausea,

vomiting, and diarrhea; renal toxicity may occur several days later. Polychlorinated biphenyls (PCBs) cross the placenta and accumulate in breast milk; exposure in utero is thought to cause behavioral problems in later life.

- 28.4 C. While all of the answers are situations or conditions that can be associated with seizure, ethanol ingestion is the most likely based on the history of a toddler with hypoglycemia poorly supervised with presumed access to alcohol after an adult party. An ingestion of MDMA can certainly cause seizure in a toddler but is usually associated with hypertension, dilated pupils, and hyperthermia. There was no evidence of trauma on exam, and the funduscopic exam did not suggest increased intracranial pressure. If insulin was in the home and Munchausen syndrome by proxy was suspected, simultaneous evaluation of serum insulin level and C peptide during an episode of hypoglycemia may help make the diagnosis.
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### CLINICAL PEARLS

- Lead-containing paint in older homes is the major source of lead exposure in the United States.
  - Behavioral signs of lead toxicity include hyperirritability, altered sleep patterns, decreased play activity, loss of developmental milestones (especially speech), and altered state of consciousness. Physical symptoms include vomiting, intermittent abdominal pain, constipation, ataxia, coma, and seizures.
  - Chelation therapy in an asymptomatic child with elevated lead levels consists of intramuscular calcium disodium ethylenediaminetetraacetic acid (CaEDTA) or oral meso-2,3-dimercaptosuccinic acid (succimer). Hospitalized patients with symptomatic disease are often treated with 2,3-dimercaptopropanol (BAL) and CaEDTA.
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## CASE 29

A 14-year-old Hispanic male presents with a 3-day complaint of “brown urine.” He has been your patient since birth and has experienced no major illnesses or injuries, is active in band and cross-country, and denies drug use



or sexual activity. Two weeks ago he had 2 days of fever and a sore throat, but he improved spontaneously and has been well since. His review of systems is remarkable only for his slightly puffy eyes, which he attributes to late-night studying for final examinations. On physical examination he is afebrile, his blood pressure is 135/90 mm Hg, he is active and nontoxic in appearance, and he has some periorbital edema. The urine dipstick has a specific gravity of 1.035 and contains 2+ blood and 2+ protein. You spin the urine, resuspend the sediment, and identify red blood cell casts under the microscope.

- ▶ What is the most likely cause of this patient's hematuria?
- ▶ What laboratory tests would support this diagnosis?
- ▶ What is the prognosis of this condition?

### ANSWERS TO CASE 29: **Acute Poststreptococcal Glomerulonephritis**

*Summary:* A healthy adolescent male with a preceding pharyngitis has periorbital edema and mild hypertension, and has developed tea-colored urine that on microscopy reveals red blood cells.

- **Most likely diagnosis:** Acute poststreptococcal glomerulonephritis (APSGN).
- **Laboratory studies:** C<sub>3</sub> (low in 90% of cases), C<sub>4</sub> (usually normal); antistreptolysin-O (ASO) enzyme antibodies and antideoxyribonuclease B (anti-DNase B) antibodies provide evidence of recent streptococcal infection.
- **Prognosis:** Excellent; 95% to 98% of affected children recover completely.

## ANALYSIS

### *Objectives*

1. Recognize the typical presentation of APSGN.
2. Know the different diagnostic possibilities for a patient with dark urine.

3. Discuss appropriate follow-up care for the patient with APSGN.

### ***Considerations***

This patient is otherwise healthy, had pharyngitis, and now has hematuria, proteinuria, edema, and hypertension. Although APSGN is likely, other possibilities must be considered. Strenuous activity can cause rhabdomyolysis and dark urine, but patients with these conditions often will have muscle aches, fatigue, nausea and vomiting, and fever. Immunoglobulin A (Berger) nephropathy is characterized by recurrent painless hematuria, usually preceded by an upper respiratory tract infection. Henoch-Schönlein purpura (HSP) is a relatively common cause of nephritis in pediatrics, but most cases occur in younger children, peaking in incidence between 4 and 5 years of age. Lupus nephritis (systemic lupus erythematosus [SLE]) can present as described and is considered if the hematuria does not resolve or if the C<sub>3</sub> level does not normalize in 6 to 12 weeks.

APPROACH TO:

**Acute Poststreptococcal Glomerulonephritis**

## **DEFINITIONS**

**GLOMERULONEPHRITIS:** Glomerular inflammation resulting in the triad of hematuria, proteinuria, and hypertension.

**RED CELL CASTS:** Injured glomeruli have increased permeability and leak red cells and proteins into the proximal convoluted tubule; the material subsequently clumps in the distal convoluted tubule and in the collecting ducts. When passed, these cell clumps retain the shape of the tubule in the urine. Red cell casts are markers for glomerular injury.

## **CLINICAL APPROACH**

**Acute poststreptococcal glomerulonephritis (APSGN) is the most common of the postinfectious nephritides**, comprising 80% to 90% of cases. Other bacteria, viruses, parasites, and fungi also have been implicated. Males are more commonly affected; it is most common in children between the ages of 5 and 15 years and is rare in toddlers and infants. The group A  $\beta$ -

hemolytic *Streptococcus* (GABHS) infection can be in the form of either pharyngitis (“strep throat”) or a superficial skin lesion (impetigo). Not all GABHS infections result in APSGN; certain GABHS strains are “nephritogenic” and are more likely to result in APSGN. Rheumatic fever only rarely occurs concomitantly with APSGN. **Antibiotic use during the initial GABHS infection may reduce the subsequent rheumatic fever risk, yet has not been shown to prevent APSGN.** The nephritis risk after infection with a nephritogenic strain of GABHS remains 10% to 15%.

**Generally the interval between GABHS pharyngitis and APSGN is 1 to 2 weeks;** the interval between GABHS impetigo and APSGN is 3 to 6 weeks. Symptom onset is abrupt. Although almost all patients have **microscopic hematuria**, only 30% to 50% develop gross hematuria. In addition, 85% present with edema and 60% to 80% develop hypertension.

The **most important laboratory test** in patients with APSGN is measurement of serum  $C_3$  and  $C_4$  levels.  $C_3$  is low in 90% of APSGN cases, whereas  $C_4$  **usually is normal**. If both levels are low, an alternate diagnosis is considered. Urinalysis typically reveals high specific gravity, low pH, hematuria, proteinuria, and red cell casts. Documentation of a recent streptococcal infection is helpful; **serum markers include the presence of ASO enzyme antibodies and anti-DNase B antibodies.** ASO antibodies are found in 80% of children with recent GABHS pharyngitis but in less than 50% of children with recent GABHS skin infection. ASO titers are positive in 16% to 18% of normal children. **Anti-DNase B antibodies assays are more reliable;** they are present in almost all patients after GABHS pharyngitis and in the majority of patients after GABHS skin infection. Antibodies to other streptococcal antigens (nicotamide adenosine dinucleotide glycohydrolase [NADase], hyaluronidase, and streptokinase) may also be assayed. Renal biopsy is no longer routine. Treatment is generally supportive. Fluid balance is crucial; diuretics, fluid restriction, or both may be necessary. Sodium and potassium intake may require restriction. **Hypertension** usually is easily controlled with **calcium-channel blockers**. Strict bed rest and corticosteroid medications are not helpful. Dialysis is rarely required.

**Resolution usually is rapid and complete.** The edema resolves in 5 to 10 days, and patients usually are normotensive within 3 weeks.  $C_3$  levels usually normalize in 2 to 3 months; a persistently low  $C_3$  level is uncommon and

suggests an alternate diagnosis. Microscopic hematuria may persist for 1 to 2 years.

## COMPREHENSION QUESTIONS

- 29.1 A 16-year-old adolescent boy complains of intermittent cola-colored urine of several years' duration, usually when he has a "cold." He is otherwise well and has no medical complaints. When the dark-colored urine is present, he has no dysuria. None of his family members has similar complaints or renal disease. On physical examination he is normotensive and appears healthy. Which of the following is the most likely cause of his intermittent hematuria?
- A. Acute poststreptococcal glomerulonephritis
  - B. Henoch-Schönlein purpura nephritis
  - C. IgA nephropathy
  - D. Recurrent kidney stones
  - E. Rapidly progressive glomerulonephritis
- 29.2 The parents of a healthy 12-year-old girl bring her to you for a physical examination required for summer camp. They have no complaints, and the girl denies any problems. Her last menses was normal 2 weeks prior. The camp requires a urine screen. To your surprise, the clean-catch urine screen has significant hematuria. Red cell casts are noted. You tell the findings to the parents, and they respond that "everyone on dad's side of the family has blood in their urine and they are all doing well." The family history is negative for deafness and for renal failure. Microscopy of renal tissue from this patient or from her father will most likely reveal which of the following?
- A. Endothelial cell swelling and fibrin in the subendothelial space
  - B. Immune complex deposition in the mesangium
  - C. Large numbers of crescentic glomeruli
  - D. Renal cell carcinoma
  - E. Thinning of the basement membrane

29.3 A 17-year-old adolescent female has joint tenderness for 2 months; the pain has affected her summer job as a lifeguard. In the morning, she awakens with bilateral knee pain and swelling, and right hand pain. The pain eases during the day but never completely resolves. Nonsteroidal anti-inflammatory drugs help slightly. She also wants a good “face cream” because “her job has worsened her acne.” On physical examination you notice facial erythema on the cheeks and nasolabial folds. She has several oral ulcers that she calls cold sores and bilateral knee effusions, and her right distal interphalangeal joints on her hand are swollen and tender. Her liver is palpable 3 cm below the costal margin. She has microscopic hematuria and proteinuria. Which of the following is the most likely cause of this young woman’s arthritis?

- A. Juvenile rheumatoid arthritis
- B. Lyme disease
- C. Osteoarthritis
- D. Postinfectious arthritis
- E. Systemic lupus erythematosus

29.4 You are not surprised to see one of your most challenging patients, a 16-year-old adolescent girl who has been seen several times per week over the last 2 months complaining of cough, occasional hemoptysis, malaise, and intermittent low-grade fever. Thus far you have identified a microcytic, hypochromic anemia for which she has been taking iron (without response) and migratory patchy infiltrates on chest radiograph that seem unaffected by antibiotic treatment. She has no tuberculosis (TB) exposure risks, and her TB skin test was negative. Today she also complains of facial edema and tea-colored urine. You suddenly realize her symptoms can be grouped as which of the following syndromes?

- A. Alport syndrome
- B. Denys-Drash syndrome
- C. Goodpasture syndrome
- D. Hemolytic-uremic syndrome
- E. Nephrotic syndrome

## ANSWERS

- 29.1 C. Recurrent painless gross hematuria, frequently associated with an upper respiratory tract infection, is typical of IgA nephropathy. These patients may develop chronic renal disease over decades. If proteinuria, hypertension, or impaired renal function were found, a biopsy would be necessary. The other options are not consistent with the asymptomatic, intermittent nature of this patient's problem.
- 29.2 E. This history is consistent with benign familial hematuria, an autosomal dominant condition that causes either persistent or intermittent hematuria without progression to chronic renal failure. Biopsy reveals a thin basement membrane; in some cases the biopsy is normal. Immune complex deposition with immunoglobulin (Ig) A in the mesangium is seen in HSP and IgA nephropathy; endothelial cell swelling with fibrin deposition is seen in hemolytic-uremic syndrome, and crescentic glomeruli are seen in rapidly progressive glomerulonephritis.
- 29.3 E. Systemic lupus erythematosus affects more women than men, and nephritis is a common presenting feature. Her rash, photosensitivity, oral ulcers, hepatomegaly, arthritis, and nephritis combine to make this a likely diagnosis. A positive antinuclear antibody test and low C<sub>3</sub> and C<sub>4</sub> levels would help to confirm the diagnosis.
- 29.4 C. Goodpasture syndrome is the clinical diagnosis when patients exhibit nephritis and pulmonary hemorrhage. It can be caused by a number of conditions, including SLE and HSP. Alport syndrome is a genetic defect in collagen synthesis that leads to abnormal basement membrane formation; patients will develop hematuria, proteinuria, and renal failure. Denys-Drash syndrome is a group of findings composed of Wilms tumor, gonadal dysgenesis, and nephropathy.
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### CLINICAL PEARLS

- Poststreptococcal glomerulonephritis is the most common postinfectious nephritis and has a good prognosis.
  - Confirming the diagnosis of APSGN requires evidence of invasive streptococcal infection such as an elevated anti-DNase B titer.
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### CASE 30

Parents bring their 5-year-old daughter to your clinic because she has developed breast and pubic hair over the past 3 months. Physical examination

reveals a girl whose height and weight are above the 95th percentile, Tanner stage II breast and pubic hair development, oily skin, and facial acne.

- ▶ What is the most likely diagnosis?
- ▶ What is the best next step in the evaluation?

### ANSWERS TO CASE 30: **Precocious Puberty**

*Summary:* A 5-year-old girl has breast and pubic hair development, tall stature, and facial acne.

- **Most likely diagnosis:** Idiopathic central precocious puberty.
- **Next step in the evaluation:** Inquire about birth history, illnesses, hospitalizations, medications, siblings' health status, and family history of early puberty and diseases. Serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels and bone age radiographs are helpful.

## ANALYSIS

### *Objectives*

1. Understand the underlying causes of precocious puberty.
2. Describe laboratory and radiologic tests that are helpful in determining the etiology of precocious puberty.
3. Establish the treatment and follow-up necessary for a child with precocious puberty.

### *Considerations*

This 5-year-old girl has precocious puberty signs (breast and pubic hair development and tall stature). She may have true (central) precocious puberty or precocious (non-central) pseudopuberty. A central nervous system (CNS) cause of true precocious puberty must be ruled out because she is younger than 6 to 8 years, and a CNS cause must be ruled out in boys at any age below ~9 years.

APPROACH TO:



## Precocious Puberty

### DEFINITIONS

**DELAYED PUBERTY:** No signs of puberty in girls by the age of 13 years or in boys by the age of 14 years. May be caused by gonadal failure, chromosomal abnormalities (Turner syndrome, Klinefelter syndrome), hypopituitarism, chronic disease, or malnutrition.

**PRECOCIOUS PUBERTY:** Secondary sexual characteristic onset before age 6 to 8 years in girls and 9 years in boys. Children in different ethnic groups undergo puberty differently; African-American girls often do so earlier than Caucasian girls.

**TRUE (CENTRAL) PRECOCIOUS PUBERTY:** Gonadotropin-dependent. Hypothalamic-pituitary-gonadal activation leading to secondary sex characteristics.

**PRECOCIOUS (NONCENTRAL) PSEUDOPUBERTY:** Gonadotropin-independent. No hypothalamic-pituitary-gonadal activation. Hormones usually are either exogenous (birth control pills, estrogen creams) or from adrenal/ovarian tumors.

**PREMATURE ADRENARCHE:** Early activation of adrenal androgens (typically in girls ages 6 to 8 years), with gradually increasing pubic/axillary hair development and body odor.

**PREMATURE THELARCHE:** Early breast development (typically in girls ages 1 to 4 years), without pubic/axillary hair development or linear growth acceleration.

### CLINICAL APPROACH

**More common in girls, true precocious puberty stems from secretion of hypothalamic GnRH** with normal-appearing, but early, progression of pubertal events. Sexual precocity is **idiopathic in more than 90% of girls**, whereas a **structural CNS abnormality is present in 25% to 75% of boys**.

Girls with gonadotropin-independent, precocious pseudopuberty have an independent source of estrogens causing their pubertal changes. An exogenous

source of estrogen (birth control pills, hormone replacement) or an **estrogen-producing tumor of the ovary or adrenal gland** must be considered. **CNS lesions** causing precocious puberty without neurologic symptoms are rarely malignant and seldom require neurosurgical intervention.

A detailed history offers important clues regarding the onset of puberty. Three main patterns of precocious pubertal progression can be identified, particularly in girls. Most girls who are younger than 6 years at onset have rapidly progressing sexual precocity, characterized by early physical and osseous maturation with a loss of ultimate height potential. Girls older than 6 years typically have a slowly progressing variant with parallel advancement of osseous maturation and linear growth and preserved height potential. In a small percentage of girls, there is spontaneous regression or unsustained central precocious puberty at a young age, with normal pubertal development at an expected age.

A neurologic history may identify past hydrocephalus, head trauma, meningoencephalitis, or the presence of headaches, visual problems, or behavioral changes. The type, sequence, and age at which pubertal changes were first noticed (breast and pubic/axillary hair development, external genitalia maturation, menarche) give valuable information regarding the etiology of the problem. Important questions include the following:

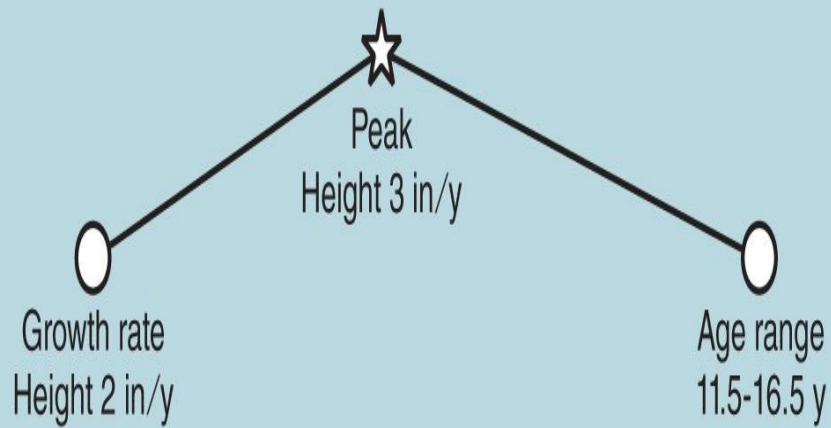
- Has the child been rapidly outgrowing shoes and clothes (evidence of linear growth acceleration)?
  - Has the child's appetite increased?
  - Has the child developed body odor?
  - Was the child possibly exposed to an exogenous source of sex steroids (oral contraceptives, hormone replacement, anabolic steroids)?
  - At what ages did parents and siblings undergo puberty?
- Is there a known or suspected family history of congenital adrenal hyperplasia?

Physical examination offers further important information ([Figures 30-1](#) and [30-2](#)). Serial height measurements are critical for determining the child's growth velocity.

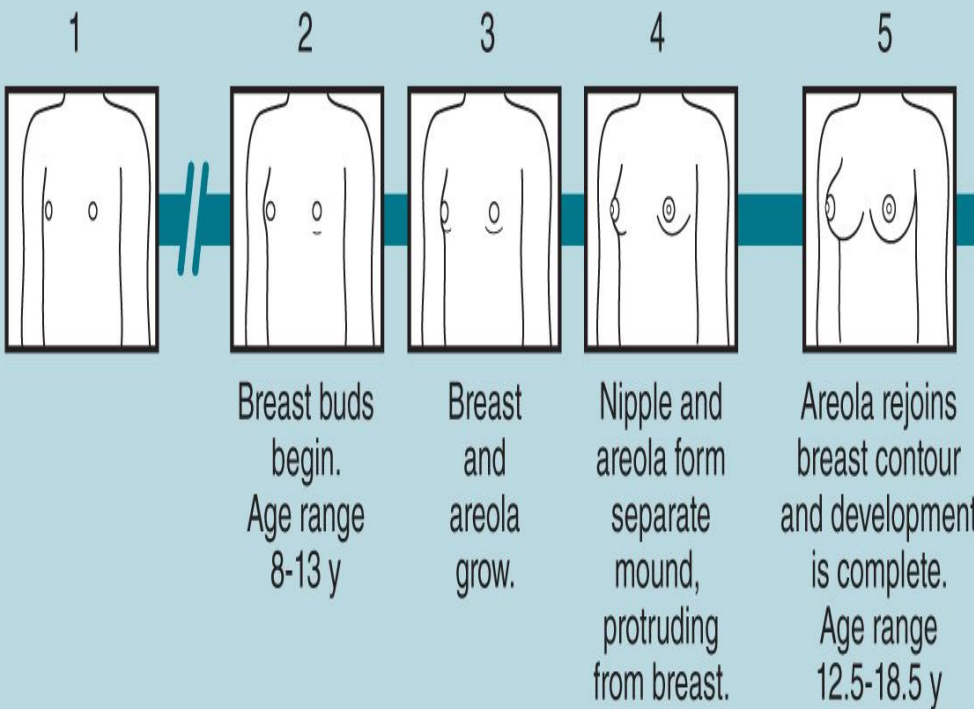
## Girls

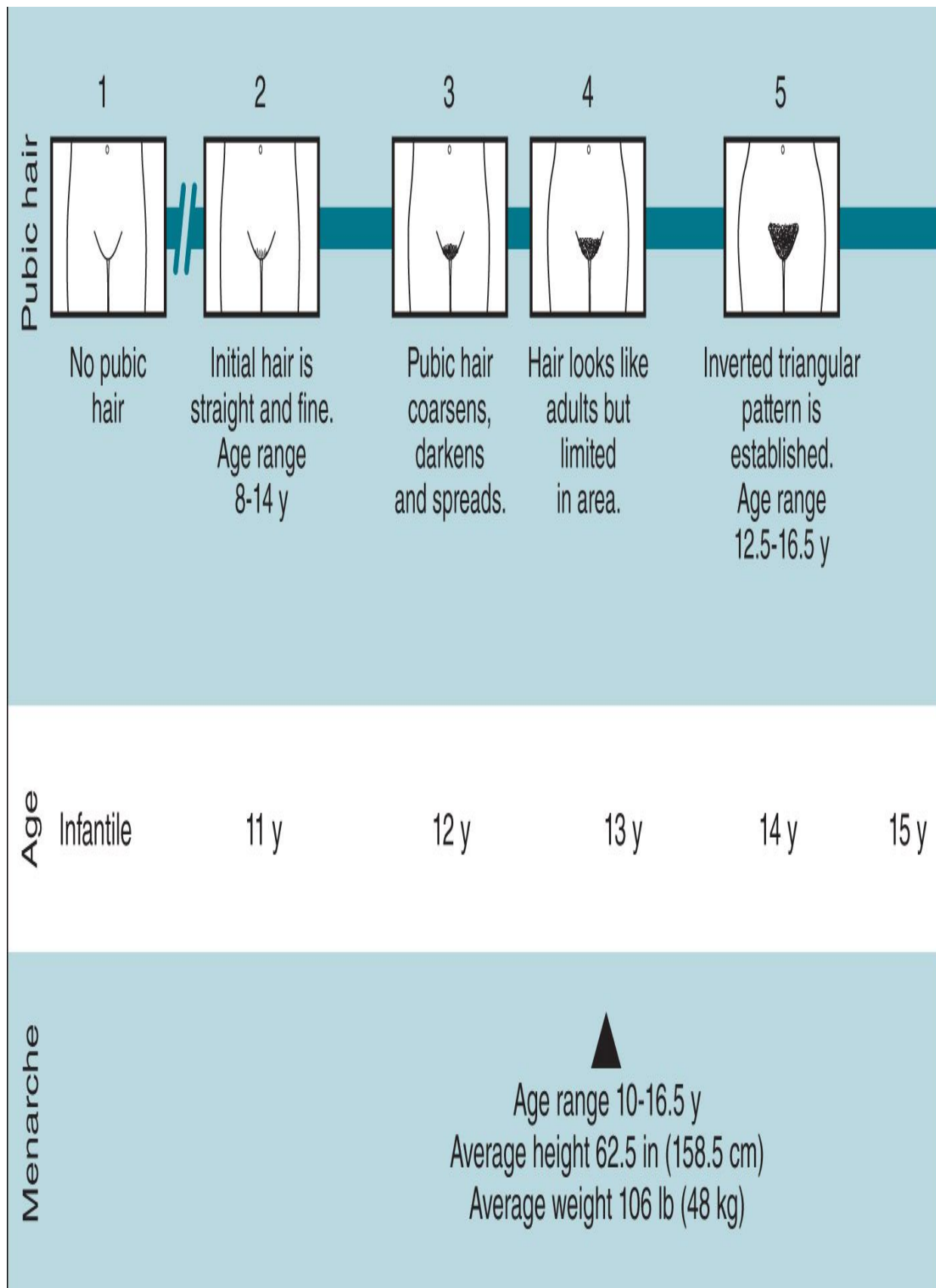
### Tanner Stage

Height  
spurt



Breast



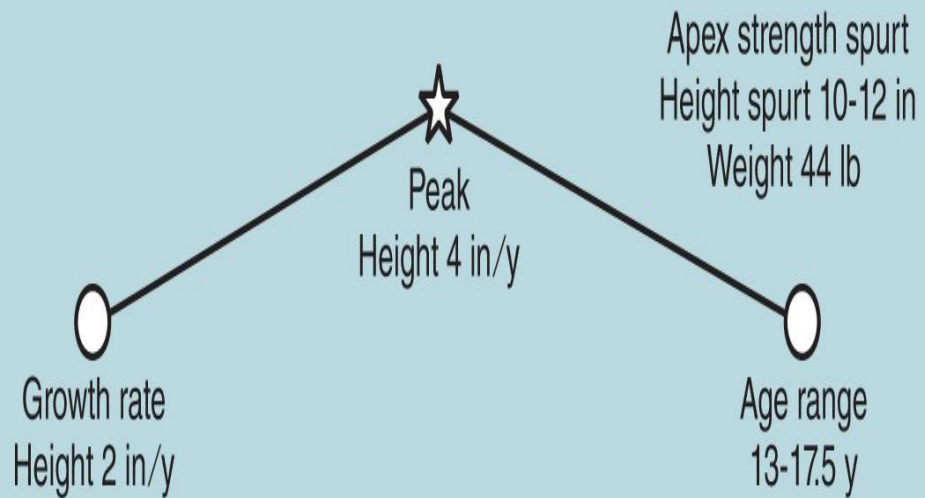


**Figure 30-1.** Female Tanner staging.

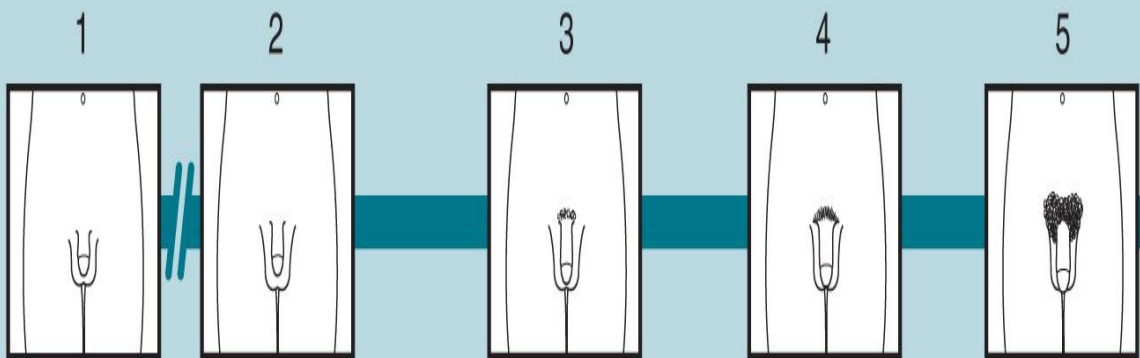
## Boys

### Tanner Stage

Height  
spurt



Penis/Testes

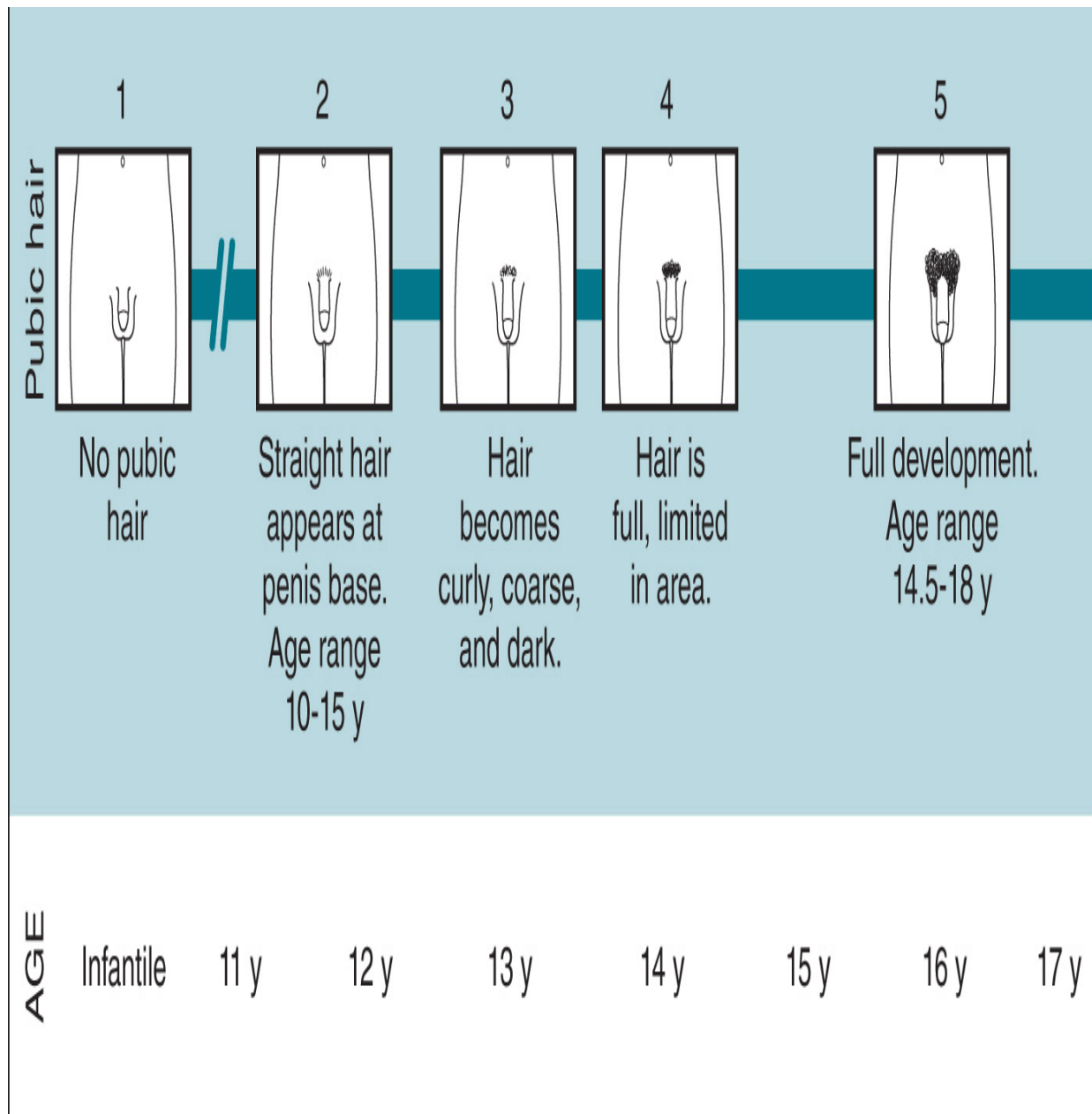


Testes increase  
in size and  
skin of scrotum  
reddens.  
Age range  
10-13.5 y

Penis grows  
in length.

Penis grows  
in width.

Development  
is complete.  
Age range  
14.5-18 y



**Figure 30-2.** Male Tanner staging.

The skin should be examined for café-au-lait spots (neurofibromatosis, McCune-Albright disease), oiliness, and acne. The presence of axillary hair and body odor, the amount of breast tissue, and whether the nipples and areolae are enlarging and thinning are documented. The amount, location, and character of pubic hair should be noted. The abdomen is palpated for masses. Boys are examined for enlargement of the penis and testes ( $>2.5$  cm in precocious puberty) and thinning of the scrotum (prepubertal scrotum is thick

and nonvascular). If the testes are different in size and consistency, a unilateral mass is considered. Testicular transillumination may be helpful. In girls, the clitoris, labia, and vaginal orifice are examined to identify vaginal secretions, maturation of the labia minora, and vaginal mucosa estrogenization (dull, gray-pink, and rugaed rather than shiny, smooth, and red). A neurologic examination also is performed.

In precocious puberty, serum sex hormone concentrations usually are appropriate for the observed stage of puberty, but inappropriate for the child's chronologic age. Serum estradiol concentration is elevated in girls, and serum testosterone level is elevated in boys with precocious puberty. Because LH and FSH levels fluctuate, single samples often are inadequate. An immunometric assay for LH is more sensitive than the radioimmunoassay when using random blood samples; with this test, serum LH is undetectable in prepubertal children, but is detectable in 50% to 70% of girls (and an even higher percentage of boys) with central precocious puberty. A gonadotropin-releasing hormone (GnRH) stimulation test, measuring response time and peak values of LH and FSH after intravenous administration of GnRH, is a helpful diagnostic tool.

**Bone age radiographs are advanced beyond chronologic age in precocious puberty.** Organic CNS causes of central sexual precocity are ruled out by computed tomography (CT) or magnetic resonance imaging (MRI), particularly in girls younger than 6 years and in all boys. Pelvic ultrasonography is indicated if gonadotropin-independent causes of precocious puberty (ovarian tumors/cysts, adrenal tumors) are suspected based on examination.

The goal of treating precocious puberty is to prevent premature closure of the epiphyses, allowing the child to reach full adult growth potential. Gonadotropin-releasing hormone agonists are used for treatment of central precocious puberty. These analogues desensitize the gonadotropic cells of the pituitary to the stimulatory effect of GnRH produced by the hypothalamus. Nearly all boys and most girls with rapidly progressive precocious puberty are candidates for treatment. Girls with slowly progressive puberty do not seem to benefit from GnRH agonist therapy in adult height prognosis. A pediatric endocrinologist should evaluate children considered for GnRH agonist treatment.



## COMPREHENSION QUESTIONS

- 30.1 A 5-year-old girl has bilateral breast development that was first noticed 6 months ago. She takes no medications, and no source of exogenous estrogen is present in the home. Family history is unremarkable. Physical examination reveals a girl who is at the 50th percentile for height and weight, with normal blood pressure, normal skin without oiliness, Tanner stage II breasts, soft abdomen without palpable masses, no body odor, no pubic/axillary hair, and mild estrogenization of the vagina. Which of the following is the most likely explanation for the child's breast development?
- A. Adrenal tumor
  - B. Central precocious puberty
  - C. Congenital adrenal hyperplasia
  - D. Premature adrenarche
  - E. Premature thelarche
- 30.2 A 4-year-old boy has started growing pubic hair and has recently exhibited aggressive "bullying" behavior at his preschool. History reveals the boy to be a term infant without postnatal complications. The child takes no medications. Family history is unremarkable. He has one younger sister who is well. Physical examination reveals height and weight above the 95th percentile, marked muscular development, Tanner stage II pubic hair development, scant axillary hair, prepubertal testicular size, a masculine voice, and oily skin. The abdominal examination is normal. The child's bone age is 6 years. Which of the following is the most appropriate next step in management?
- A. Brain MRI
  - B. Dexamethasone challenge test
  - C. Reassure the family that no studies are needed
  - D. Serum  $17\alpha$ -hydroxyprogesterone level
  - E. Testicular ultrasound
- 30.3 A mother brings to your clinic her 13-year-old daughter who is "falling behind" in growth and who has not yet exhibited pubertal changes.

Physical examination reveals a height less than the 5th percentile, no signs of secondary sexual characteristics, a small mandible, low posterior hairline, prominent ears, and a broad chest. Which of the following is the most appropriate next step in management?

- A. Abdominal ultrasound
- B. Bone age radiograph
- C. Chromosome analysis
- D. Reassure the family and recommend height measurement in 6 months
- E. Treat with growth hormone injections

**30.4** A father brings his 14-year-old son to your clinic because his teacher has concerns about his poor school performance and maladjusted behavior. He has poor grades in all subjects, is extremely shy, and has always had difficulty in adjusting socially. On examination, he is at the 95th percentile for height and 5th percentile for weight. It is very difficult to engage him in conversation. The testes are prepubertal, he has mild hypospadias, and he has no secondary sexual characteristics. Which of the following is the most likely cause of his pubertal delay?

- A. Hypopituitarism
- B. Klinefelter syndrome
- C. Marfan syndrome
- D. Noonan syndrome
- E. Testicular tumor

## ANSWERS

**30.1 E.** All of this child's findings are estrogen related. She has no virilization. Postulated premature thelarche causes include ovarian cysts and transient gonadotropin secretion. No treatment is necessary.

**30.2 D.** Boys with congenital adrenal hyperplasia have virilization despite prepubertal testicles. This results from a disorder of steroid synthesis, leading to a deficiency of cortisol and an overproduction of androgenic intermediary metabolites such as  $17\alpha$ -hydroxyprogesterone.

- 30.3 C. This child has Turner syndrome (45, XO). Other features include webbed neck, high arched palate, increased nevi, renal anomalies, increased arm-carrying angle, and edema of the hands and feet. Treatment includes recombinant human growth hormone and estrogen replacement therapy.
- 30.4 B. Klinefelter syndrome (47,XXY) usually comes to attention because of gynecomastia and small testes. These males usually are clinically normal at birth. Treatment involves replacement therapy with a long-acting testosterone beginning at age 11 to 12 years.
- 

### CLINICAL PEARLS

- True precocious puberty is the onset of secondary sexual characteristics before the age of 8 years in girls and 9 years in boys. It stems from secretion of hypothalamic gonadotropin-releasing hormone and is more common in girls.
  - Precocious puberty is idiopathic in more than 90% of girls, and a structural central nervous system abnormality is noted in 25% to 75% of boys.
  - When compared to norms, the serum estradiol level is elevated in girls and the testosterone level is elevated in boys with precocious puberty. Bone age radiographs are advanced beyond chronologic age.
  - The goal of treating precocious puberty is to prevent premature closure of the epiphyses, allowing the child to reach full adult growth potential.
- 

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## CASE 31

A 3740-g infant is delivered vaginally after an uncomplicated 38-week gestation. Health-care providers have immediate difficulty in determining whether the infant is a boy or girl. There appear to be small scrotal sacs that resemble enlarged labia and no palpable testes, with either a microphallus and hypospadias or an enlarged clitoris. No vaginal opening is apparent. The remainder of the examination is normal.

- What is the most likely diagnosis?
- What is the next step in evaluation?

### ANSWERS TO CASE 31: Ambiguous Genitalia

*Summary:* A full-term newborn has ambiguous genitalia.

- **Most likely diagnosis:** Congenital adrenal hyperplasia (CAH).
- **Next step in evaluation:** Karyotype, serum electrolyte levels, and serum 17 $\alpha$ hydroxyprogesterone level.

## ANALYSIS

### *Objectives*

1. Understand the underlying causes of ambiguous genitalia.
2. Describe factors that influence gender assignment in infants with ambiguous genitalia.
3. Describe the treatment and follow-up of infants after gender assignment.

## ***Considerations***

**This neonate with sexual ambiguity represents a psychosocial emergency.** Upon proper gender assignment for rearing and appropriate medical management, individuals born with ambiguous genitalia should be able to lead well-adjusted lives and satisfactory sex lives. Making a correct diagnosis as early as possible is critical. **Gender assignment** in the neonate born with sexual ambiguity should be influenced by the possibility of achieving **unambiguous and sexually useful genital structures.** Clear and comprehensive discussions with the parents, focusing on their understanding, anxieties, and religious, social, and cultural beliefs, are critical for an appropriate gender assignment. Once gender is assigned, it should be reinforced by appropriate surgical, hormonal, and psychological measures.

APPROACH TO:

**Child with Ambiguous Genitalia**

## **DEFINITIONS**

**CONGENITAL ADRENAL HYPERPLASIA (CAH):** Autosomal recessive disorder of adrenal steroid production with an enzymatic deficiency (usually 21-hydroxylase) causing inadequate production of cortisol, excessive production of androgenic intermediary metabolites, and virilization.

**HERMAPHRODITISM:** Discrepancy between gonad morphology and external genitalia.

**INTERSEX STATE:** Infant with ambiguous genitalia.

**MICROPHALLUS:** Penis size below the fifth percentile for age; neonate with a stretched penile length of less than 2 cm.

**VIRILIZATION:** Masculinization where infant girls exhibit clitoromegaly, labial fusion, and labial pigmentation; infant boys usually appear normal.

## **CLINICAL APPROACH**

Evaluation of the infant with ambiguous genitalia must occur rapidly to alleviate family anxiety. An endocrinologist, clinical geneticist, urologist, and

psychiatrist are essential members of the intersex evaluation team. The **goals of the evaluation** are to determine the **etiology** of the intersex problem, **assign gender**, and **intervene with surgical or other treatment** as soon as possible. Intersex abnormalities include the following:

**Female pseudohermaphroditism:** 46,XX karyotype; largest neonatal group with ambiguous genitalia; predominant etiology is CAH; rarer etiologies include exposure to maternal androgens/progestins and congenital vaginal absence with uterine absence or abnormality; degree of masculinization depends on stage of development at time of androgenic stimulation and potency and duration of exposure.

**Male pseudohermaphroditism:** 46,XY karyotype; etiologies include testosterone dyssynthesis, 5 $\alpha$ -reductase/dihydrotestosterone deficiency, and decreased androgen binding to target tissues (androgen insensitivity syndrome most common form of male pseudohermaphroditism); phenotypically normal females with functioning testicular tissue, variable incomplete virilization of genitalia, and short, pouchlike vaginas; typically diagnosed at puberty when primary amenorrhea noted; maintain as females and offer vaginoplasty.

**True hermaphroditism:** About 70% 46,XX and remainder 46,XY or mosaic; comprises less than 10% of all intersex cases; bilateral ovotestes or ovary and testis on opposite sides; testicular tissue determines virilization degree; gender assignment based on genitalia appearance (approximately 75% assigned male gender); contradictory reproductive structures removed in older patients with assigned gender.

**Mixed gonadal dysgenesis:** Most 46,XY/45, XO karyotype; testis with Sertoli and Leydig cells, but no germinal elements, on one side and streak gonad on other; hypospadias, partial labioscrotal fusion, and undescended testes most common (incompletely virilized male appearance); usually assigned female gender and undergo gonadectomy (25% of streak gonads develop malignancy); assign as male if testes descended.

### ***Assessment***

After obtaining a careful history, a family pedigree should be constructed to identify consanguinity and to document cases of genital ambiguity, infertility, unexpected pubertal changes, or inguinal hernias. Physical findings could support a genetically transmitted intersex condition. The history of an

unexplained neonatal death may suggest a family history of CAH. Maternal exposure to endogenous or exogenous androgens should be investigated.

A thorough physical examination is crucial in determining the diagnosis and making the most reasonable gender assignment. A critical physical finding is the presence or absence of a testis in a labioscrotal compartment. Other physical findings include hyperpigmentation of the labioscrotal folds (common in infants with CAH); phallic size and location of urethral opening; palpation of a uterus on bimanual examination; evidence of failure to thrive (failure to regain birth weight, progressive weight loss, vomiting); and dehydration. **Phallic size is the most important factor in determining an infant's sex assignment.**

**Karyotype analysis using activated lymphocytes is an important first step in the laboratory evaluation of infants with ambiguous genitalia.** Results with a high degree of accuracy can be available in less than 72 hours. To determine mosaicism, repeat studies on multiple tissues may be necessary. If CAH is suspected, biochemical studies might include a **serum 17 $\alpha$ -hydroxyprogesterone level**. Plasma testosterone levels alone usually are not helpful. Urinary steroids and plasma androgens, measured before and after administration of corticotropin (adrenocorticotrophic hormone [ACTH]) and human chorionic gonadotropin (hCG), help to determine whether a block in testosterone synthesis or 5 $\alpha$ -reductase deficiency exists.

An ultrasonogram or pelvic magnetic resonance imaging (MRI), urogenital sinus x-ray after contrast injection, and fiberoptic endoscopy may also aid in the evaluation. Laparoscopy usually is not necessary in the newborn because primary emphasis is placed on the external genitalia and the possibilities for adequate sexual function in assigning gender.

### ***Treatment***

The major treatment consideration for infants with ambiguous genitalia is the possibility of achieving cosmetically and functionally normal external genitalia by surgical and hormonal means. **Because the presence of ambiguous external genitalia may reinforce doubt about the sexual identity of the infant, reconstructive surgery is performed as early as medically and surgically feasible, usually before 6 months of age.**

Feminizing genitoplasty is the most common surgical procedure performed in female pseudohermaphrodites, in true hermaphrodites, and in male

pseudohermaphrodites reared as females. The goal of this surgery is to reduce the size of the clitoris while maintaining vascularity and innervation, feminizing the labioscrotal folds, and ultimately creating a vagina. Because of the high incidence of gonadal tumors in individuals with certain forms of gonadal dysgenesis, gonadectomy performed concurrently with the initial repair of the external genitalia is mandatory. **A male with hypospadias often requires multiple procedures to create a phallic urethra. Circumcision is avoided** in these individuals because the foreskin tissue is commonly used for reconstruction.

If steroid production is the underlying etiology of the intersex problem, treatment is provided to prevent further virilization. **Administration of hydrocortisone to individuals with CAH helps to inhibit excessive production of androgens and further virilization.** Hormone substitution therapy in hypogonadal patients is prescribed so that secondary sexual characteristics develop at the expected time of puberty. Oral estrogenic hormone substitution is initiated in females, and repository injections of testosterone are given to males. With the exception of some female pseudohermaphrodites and true hermaphrodites reared as females, disorders that cause ambiguous genitalia usually lead to infertility.

## COMPREHENSION QUESTIONS

- 31.1 A 3650-g term infant has ambiguous genitalia, including an enlarged clitoris or microphallus and one palpable testis in the labioscrotal folds. Sonogram reveals a uterus and ovaries. Which of the following is the most likely explanation for the child's ambiguous genitalia?
- A. Aromatase deficiency
  - B. Congenital adrenal hyperplasia
  - C. Female pseudohermaphroditism
  - D. Male pseudohermaphroditism
  - E. True hermaphroditism
- 31.2 A mother brings in her 1-week-old son who has vomited four times over the last 24 hours. He has no fever or diarrhea. The infant is breast-feeding poorly and is "floppy" per the mother. He has had only one wet diaper in the last 12 hours. Physical examination reveals a lethargic



infant who has lost 250 g since birth, with pulse of 110 bpm, dry oral mucosa, and no skin turgor. Which of the following levels should be checked after stabilization and electrolyte measurement?

- A. Serum cortisol
- B. Urine cortisol
- C. Serum 21-hydroxylase
- D. Serum  $17\alpha$ -hydroxyprogesterone
- E. Serum testosterone

31.3 A mother brings in her 15-year-old daughter because she has never started her periods. She otherwise is healthy and takes no medications. Her past medical history is unremarkable except for inguinal hernia repair as an infant. Family history is unremarkable. She is at the 75th percentile for height and weight, has Tanner stage IV breast development, and no pubic or axillary hair development. Her anogenital examination reveals a short, pocketlike vaginal opening. Which of the following is the most likely explanation for her amenorrhea?

- A. Adrenal tumor
- B. Congenital adrenal hyperplasia
- C. Pituitary tumor
- D. Testicular feminization
- E. Turner syndrome

31.4 You examine a full-term 3780-g newborn in the nursery and notice that he has marked hypotonia, a very small penis, and unilateral cryptorchidism. Which of the following is the most likely explanation for these findings?

- A. Congenital adrenal hyperplasia
- B. Male pseudohermaphroditism
- C. Maternal treatment with steroids
- D. Mixed gonadal dysgenesis
- E. Prader-Willi syndrome

## ANSWERS

- 31.1 **E.** The gonad in the labioscrotal fold suggests a testis, but a uterus and an ovary on sonography are highly suggestive of a true hermaphrodite. Gender assignment in this case should be based on the possibility of surgical correction of the external genitalia. Assignment of female sex and an attempt to preserve ovarian tissue is appropriate.
- 31.2 **D.** Male infants with salt-losing CAH develop clinical symptoms similar to pyloric stenosis, intestinal obstruction, heart disease, cow's milk intolerance, and other causes of failure to thrive. Their genitalia appear normal. A serum 17 $\alpha$ -hydroxyprogesterone level typically is elevated. Without appropriate treatment (hydrocortisone, mineralocorticoid, and sodium supplementation), cardiovascular collapse and death may occur within a few weeks. Many states have neonatal screening programs for CAH, yet infants with salt-losing CAH (21-hydroxylase deficiency) can become very ill and die before the screening results are known.
- 31.3 **D.** Testicular feminization results from decreased androgen binding to target tissues or androgen insensitivity. Patients have 46,XY karyotypes, yet appear as phenotypically normal females with a short or atretic vagina. Androgen insensitivity is the most common form of male pseudohermaphroditism. Maintaining female gender assignment is appropriate, and vaginoplasty is frequently needed after puberty.
- 31.4 **E.** Although severe hypotonia, failure to thrive, and hypogonadism characterize Prader-Willi syndrome in early life, hyperphagia, obesity, mental retardation, and the appearance of bizarre behavior manifest by the age of 6 years. Morbid obesity, limited sexual function, and severe behavioral abnormalities may occur. Mixed gonadal dysgenesis is a reasonable choice given the unilateral cryptorchidism and hypogonadism, but severe hypotonia usually is not a finding in that disorder.
- 

## CLINICAL PEARLS

- The goal of evaluating a neonate with sexual ambiguity is to determine the etiology of the intersex problem, assign gender, and intervene with surgical or other treatment as soon as possible.
- Treatment of sexual ambiguity is directed toward achieving cosmetically and functionally normal external genitalia by surgical and hormonal means.

- Reconstructive surgery for a patient with ambiguous genitalia is performed as early as medically and surgically feasible, usually before the age of 6 months.
- 

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## CASE 32

A 15-year-old boy presents to your clinic with a 3-day history of a sore on his penis. He denies urinary frequency, change in urine appearance, or penile discharge. He reports no significant past medical history. He is sexually active and infrequently uses condoms. His examination is normal, other than a shallow, nontender ulcer approximately 1 cm in diameter on the dorsal aspect of the penile shaft. There is no lesion discharge or bleeding, but slight induration around the ulcer is noted. His urinalysis is normal.

- ▶ What is the most likely diagnosis?
- ▶ What is the next step in evaluation?

## ANSWERS TO CASE 32: **Primary Syphilis**

*Summary:* A sexually active adolescent with a penile chancre.

- **Most likely diagnosis:** Primary syphilis.
- **Next step in evaluation:** Obtain a thorough history and review of systems, focusing on sexual history and symptoms consistent with sexually transmitted disease (STD) and possible extragenital infection. Perform a focused examination for oropharyngeal, abdominal, genitourinary (GU), joint, or skin abnormalities. Test for syphilis, and testing for concomitant STDs (gonorrhea, chlamydia, HIV) is always considered.

## ANALYSIS

### *Objectives*

1. Describe the workup and treatment of primary syphilis.
2. Understand the various stages of untreated syphilis.
3. Describe select ulcerative GU lesions and adolescent STDs.

### *Considerations*

This adolescent with a painless penile ulcer represents a typical presentation for primary syphilis. Presenting symptoms and examination findings may permit narrowing the list of possible STD pathogens, but the causative agents frequently coexist and physical signs often overlap. An accurate diagnosis without testing is difficult. Considerations include sending blood, urine, urethral secretions, or a lesion aspirate or scraping for specific infections based on symptoms and examination findings. For instance dark field microscopy of an ulcer scraping may occasionally be used to diagnose syphilis while a urine chlamydia probe might be useful for a patient with dysuria, clear urethral discharge, and leukocyte esterase on urinalysis. HIV and hepatitis B screening is always considered whenever an STD is suspected.

## APPROACH TO:

### The Adolescent with Primary Syphilis

## DEFINITIONS

**CHANCER:** Painless ulcer with indurated base usually caused by *Treponema pallidum*.

**CHANCROID:** Painful ulcer with exudate caused by *Haemophilus ducreyi*.

**VENEREAL DISEASE RESEARCH LABORATORY (VDRL) AND RAPID PLASMA REAGIN (RPR):** Rapid screening assays; referred to as nontreponemal testing; measure antibody to cells affected by *Treponema pallidum*; may be false positive (related to viral infection, malignancy, or autoimmune disease) or false negative (up to 25% seroreversion [SR] possible); often used to monitor treatment response (four-fold titer decrease) or define reactivation (four-fold titer increase).

**FLUORESCENT TREPONEMAL ANTIBODY ABSORPTION (FTA-ABS) AND TREPONEMA PALLIDUM PARTICLE AGGLUTINATION (TP-PA):** Organism-specific quantitative assays; referred to as treponemal testing; measures specific antibody to *Treponema pallidum*; typically used to verify infection, or repudiate nontreponemal assay false positives or negatives (seroconversion may not occur for weeks after initial infection).

## CLINICAL APPROACH

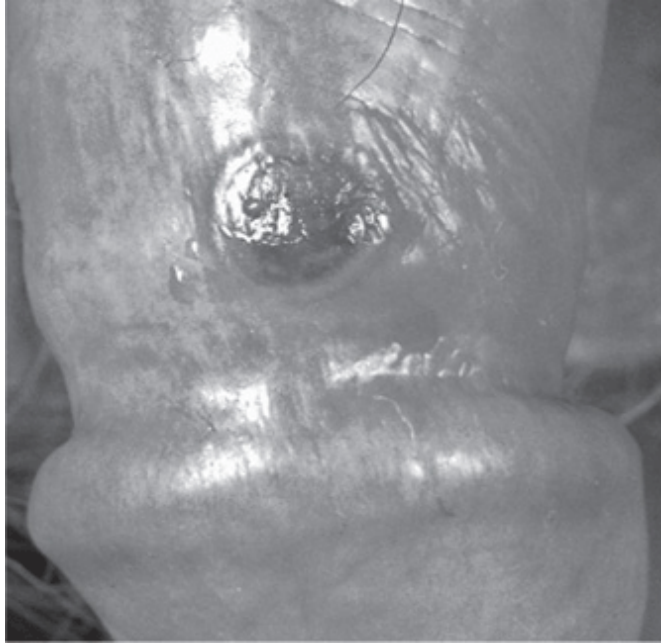
The timing and constellation of GU signs and symptoms consistent with STD can be helpful in narrowing the differential diagnosis and prompting appropriate laboratory studies and treatment. Questions should include whether **dysuria, frequency, discharge, or changes in urine appearance** have been noted. One should inquire about **lesions on the genitalia**, around the anus, or on the skin of the lower abdomen, groin, or inner thighs. Rashes elsewhere on the body also should be investigated; the transient, **pustular rash associated with disseminated gonococcal infection** or the macular rash on the palms of patients with secondary syphilis could be identified. In both sexes, typical GU infections may present atypically; gonorrhea may not

present with a purulent urethral discharge, and herpes infection could be associated with mucoid urethral discharge.

Evaluation of the **adolescent with** a penile lesion should commence with a **sexual** and **GU history** of both the patient and sexual partner(s), if known. Multiple partners, early sexual activity, inconsistent condom use, and use of drugs and alcohol are known STD risk factors. A penile chancre in an otherwise healthy, sexually active male should raise suspicion for syphilis. Urinary tract findings of dysuria and penile discharge are not typical for syphilis, but may be encountered. Inguinal lymphadenopathy also is possible.

Prevalence of syphilis in the adolescent population has been steadily increasing over the past few years, with both sexes and all racial and ethnic groups demonstrating an approximately 20% to 25% increase.

Primary syphilis is characterized by a painless ulceration that usually erupts on the genitalia or perianal region (oropharyngeal ulcer also possible) within 2 to 3 weeks of transmission, and spontaneously resolves over 4 to 6 weeks ([Figure 32-1](#)). If untreated, secondary syphilis may develop within 2 to 3 months, with malaise, fever, lymphadenopathy, and a stereotypical rash (macular to papular lesions often found on the palms and soles), or nondescript rash that may mimic an allergic dermatitis or a viral exanthem. Tertiary syphilis occurs in approximately 15% of untreated patients often a decade or more after infection, and may involve the skin (gummas), cardiovascular system (aortic aneurysm), or central nervous system (neurosyphilis with possible meningitis, seizures, or musculosensory deficits).



**Figure 32-1.** Early chancre presenting as a flat, eroded papule with raised, indurated borders and a smooth, clean base. (Reproduced, with permission, from Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ. *Fitzpatrick's Dermatology in General Medicine*, 7th ed. New York, NY: McGraw-Hill, 2007. Figure 200-2.)

Other genital ulcer diseases appearing similar to the primary syphilitic chancre include the typically painful chancroid associated with *Haemophilus ducreyi* and denuded, coalesced herpes simplex virus (HSV) lesions. Chancroid is usually characterized by an exudative and friable, but nonindurated, genital ulcer. Tender inguinal lymphadenopathy also may be noted. HSV lesions may start with localized pruritus, not typically seen with other STDs.

Initial evaluation of a patient with suspected syphilis usually involves obtaining a serum VDRL or RPR assay. If diagnostic suspicion is high, one might consider foregoing a screening assay and proceed with MHA-TP or TP-PA testing. Any neurologic symptoms or findings in the patient with suspected syphilis warrants a lumbar puncture for cell counts and VDRL or FTA-ABS testing of cerebrospinal fluid to exclude neurosyphilis.

Treatment for syphilis in the adolescent patient is dependent upon infection classification, with primary and secondary syphilis treated with one to three weekly intramuscular penicillin G injection(s), dependent on duration (unknown or greater than 1 year warrants three weekly injections). Tertiary



syphilis requires a minimum of 10 days of intravenous penicillin G. Tetracycline group antibiotics (doxycycline) are an alternative therapy consideration in the penicillin-allergic teen. Some advocate desensitizing allergic patients to and treating with penicillin, rather than using another potentially less efficacious antibiotic.

Adequate screening, timely treatment, and appropriate follow-up in syphilis are important, since a prolonged asymptomatic carrier state subsequent to the primary eruption is possible. Ultimately, a thorough history and examination, including focus on any past or present signs or symptoms consistent with GU infection, are paramount to the proper diagnosis and appropriate treatment of any STD.

## COMPREHENSION QUESTIONS

- 32.1 A 16-year-old girl presents with a 1-day history of stabbing left groin pain, and white vaginal discharge and mild dysuria for the past week. There has been no abnormal vaginal bleeding, with her last menses approximately 3 weeks ago. She reports one urinary tract infection (UTI) since menarche, but no STDs. She has been sexually active for the past year and takes an oral contraceptive. Her partners irregularly use condoms. She is afebrile, but has left lower quadrant and suprapubic abdominal pain on deep palpation and minimal guarding. Which of the following is the most appropriate next step?
- A. Request emergent surgery consultation.
  - B. Perform urinalysis and urine pregnancy testing.
  - C. Order pelvic ultrasonography.
  - D. Perform pelvic examination and Pap smear.
  - E. Order follicle-stimulating hormone and luteinizing hormone levels.
- 32.2 Over the past 2 days, a 14-year-old sexually active boy has been complaining of slight burning on urination. He has not had frequency or change in urine appearance. His past medical history is unremarkable. He is uncircumcised, and has a 1.5-cm ulcer with raised margins on his glans penis. There is no urethral erythema or discharge. The rest of his exam and a urinalysis are unremarkable. Which of the following is the



next most appropriate test to perform to diagnose his probable condition?

- A. Urine culture
- B. HIV
- C. HSV immunoglobulin G (IgG)
- D. RPR
- E. Urine GC/chlamydia probe

32.3 A 17-year-old girl presents with severe pain in the right upper quadrant and has some pain in her right shoulder. She has nausea, fever, and chills. The abdominal pain increases with movement or Valsalva activities. On physical examination, you confirm pain over the gallbladder, but also notice that she has right lower quadrant abdominal pain. Her pelvic examination is significant for discharge from the cervical os and pain upon cervical motion. Which of the following is consistent with the most likely diagnosis?

- A. Appendicitis
- B. Ectopic pregnancy
- C. Fitz-Hugh-Curtis syndrome
- D. Gallbladder disease
- E. Right lower quadrant pneumonia

32.4 A 15-year-old girl has burning on urination, but no fever, urinary frequency, hematuria, vaginal discharge, GU lesions, or abdominal pain. She has regular cycles. Her abdominal examination is normal. Her GU examination reveals erythema surrounding the vaginal introitus, but no vaginal discharge, tenderness, or masses during the pelvic examination. Her urinalysis is benign. Which of the following is the most important historical clue to be gathered?

- A. Miscarried last year
- B. Douching twice daily over the past month
- C. Treated for UTI last year
- D. Treated for chlamydia last year
- E. Receiving contraceptive injections quarterly

## ANSWERS

- 32.1 B.** STD is a concern in this patient with pyuria and abdominal pain; a surgical evaluation at this time does not seem necessary. In addition to pelvic inflammatory disease (PID), possible etiologies include UTI, ovarian torsion, ovarian cyst, and ectopic pregnancy. The first step in evaluation should be urinalysis and pregnancy testing. A pelvic examination and testing for GC and chlamydia should be included in the evaluation of this sexually active female, but a Pap smear is not likely to identify the etiology of her symptoms. Pelvic ultra-sonography may be required if the physical examination proves equivocal.
- 32.2 D.** This scenario is typical for primary syphilis. A screening urinalysis is reasonable (white blood cells or leukocyte esterase may be seen), and may help guide additional STD testing, but a urine culture is not likely to result in the correct diagnosis. Urine GC/chlamydia testing is a reasonable consideration for detecting often asymptomatic chlamydial infection, as is ordering an HIV assay whenever an STD is suspected, but initial efforts should be directed toward excluding syphilis. Finally, this case scenario is not consistent with HSV; immunoglobulin testing for HSV remains controversial with unclear diagnostic yield.
- 32.3 C.** This girl likely has Fitz-Hugh-Curtis syndrome. This disease can be seen in both genders, but is more prevalent in girls and is usually (but not always) associated with evidence of acute PID. The right upper quadrant pain results from ascending pelvic infection and inflammation of the liver capsule and diaphragm. It can mimic other abdominal emergencies and must be considered in sexually active adolescents as a diagnosis of exclusion. This condition was once thought to be caused only by *Neisseria gonorrhoeae*; *Chlamydia trachomatis* infection probably is more common. The acute phase is described above and in the question; a chronic phase of persistent right upper quadrant pain or complete resolution of symptoms can also be seen.
- 32.4 B.** Chemical urethritis as a result of frequent douching is likely in this patient. Other possible etiologies for this benign urethritis include chemical irritants (soaps), fabrics (rayon), and drying agents (powders). Past pregnancy and a history of GU disorder are important, but have less relevance in this case, especially given her benign pelvic examination

and urinalysis. Treatment typically entails eliminating the offending agent and waiting for symptoms to subside.

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### CLINICAL PEARLS

- The goals of evaluating GU complaints are to diagnose and treat infections that can threaten the viability of reproductive organs or cause extragenital or systemic infection.
  - Typical STDs may present atypically or in combination, making patient and partner history, focused examination, and case-specific testing important tools.
- 

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### CASE 33

A 10-year-old Caucasian child arrives back from her spring break trip with her father. She complains of a generalized slightly pruritic rash that involves her entire body, mostly sparing her face, scalp, and distal limbs. On examination the lesions are noted to be oval or round, about 1 cm or less in diameter, with raised edges and pinkish in color. Some of the lesions seem to have a scale, making the skin look “crinkly.” On her back, the lesions are more oval in shape and appear to align along cutaneous cleavage planes. Upon close questioning the mother, who has primary custody of the child, recalls possibly having seen a single similar lesion on her lower back while she and her daughter were preparing for the upcoming trip.

- ▶ What is the most likely diagnosis?
- ▶ What is the best management for this condition?

### ANSWERS TO CASE 33: **Pityriasis Rosea**

*Summary:* A 10-year-old with a diffuse, slightly pruritic annular rash that developed 10 days after a single large lesion was noted on her lower back.

- **Most likely diagnosis:** Pityriasis rosea.
- **Best management:** Supportive care with emollients and occasionally antihistamines if the pruritus is significant.

## ANALYSIS

### *Objectives*

1. Describe the clinical findings of pityriasis rosea.
2. Know the differential diagnosis for pityriasis rosea.
3. Explain the treatment options for pityriasis rosea.

### *Considerations*

A new rash on a child can reflect myriad conditions. The initial largish lesion on the back followed 5 to 10 days later by more widespread lesion as described suggest pityriasis rosea. In a sexually active adolescent, consideration for secondary syphilis would be an important consideration.

APPROACH TO:

**Pityriasis Rosea**

## DEFINITIONS

**GUTTATE PSORIASIS:** A variant of psoriasis, often following a streptococcal infection, whereby a sudden eruption of small round or oval psoriatic lesions on the trunk, face, and proximal limbs occurs.

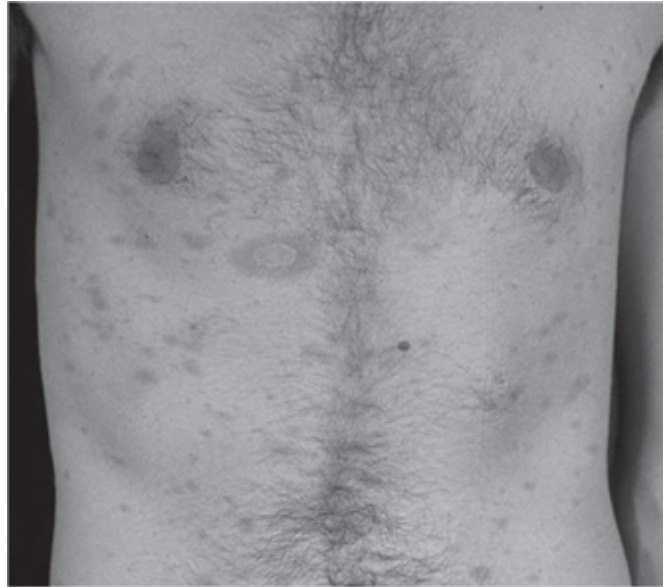
**NUMMULAR DERMATITIS:** Pruritic boggy or vesicular round lesions that erupt on the extremities, buttocks, and shoulders. When chronic, lichenification can occur.

**PITYRIASIS LICHENOIDES CHRONICA:** Multiple, small (3- to 5-mm), reddish-brown papules covered with grayish scale develop on the trunk and extremities. Its chronicity and lack of herald patch can help distinguish it from pityriasis rosea.

**PITYRIASIS ROSEA:** Benign childhood skin eruption of oval or round lesions, about 1 cm or less in diameter, with raised edges and pinkish in color, often with a scale on the surface. A “**herald patch**” is often noted 5 to 10 days prior to the generalized eruption; the generalized eruption often aligns on the back along cleavage planes, resulting in a “**Christmas tree pattern.**”

## CLINICAL APPROACH

Pityriasis rosea is a benign childhood condition. While it is occasionally preceded by a prodrome of fever and malaise, those symptoms rarely require medical attention. Rather, a single round or oval lesion of about 1 to 10 cm in size with a raised border and a scaly appearance (the “herald patch”) occurring anywhere on the body often is the harbinger of more extensive lesion development to occur in about 5 to 10 days. The lesions of the subsequent wide spread eruption occur in crops and are typically less than 1 cm in size, are oval or round, have a raised edge, and are pink to brown in color. On the back, the lesions tend to align along cutaneous cleavage lines resulting in a “Christmas tree pattern.” The herald patch is sometimes confused with a lesion of tinea corporis; a KOH scraping of this lesion will help distinguish the two ([Figure 33-1](#)).



**Figure 33-1.** Pityriasis rosea with the herald patch and the symmetric distribution on the chest. (Reproduced, with permission, from Wolff K, Johnson RA: *Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology*, 6th ed. New York, NY: McGraw-Hill; 2009. [Figure 7-1A.](#))

The cause of pityriasis rosea is unknown, but a viral etiology is suspected. The lesions last from about 2 to 12 weeks and typically are asymptomatic. Treatment consists of a bland emollient, and in the child who does have pruritus, oral antihistamines or topical corticosteroids may be required.

**Within the differential for pityriasis rosea is secondary syphilis.**

Testing for syphilis must be considered in any sexually active adolescent with suspected pityriasis rosea, especially if lesions are found on the palms or soles. Such lesions are unusual in pityriasis but common in syphilis.

Guttate psoriasis is a variant of psoriasis in which children have a sudden eruption of typical psoriasis lesions across their trunk, face, and proximal limbs. These lesions typically are small oval or round lesions that occur following a streptococcal throat or perianal infection. Antibiotic treatment for the streptococcal infection often results in marked skin improvement.

Nummular dermatitis lesions are characterized by extremely pruritic coin-sized lesions, typically on the extremities, buttocks, or shoulders. The lesions can be boggy, vesicular, and weepy or dry and scaly. They are treated similarly to atopic dermatitis, although higher-potency topical steroids are sometimes required. When these lesions occur chronically, lichenification can occur.

Pityriasis lichenoides chronica is considered a benign dermatologic condition of children whereby a generalized eruption of numerous 3- to 5-mm reddish-brown papules covered with grayish scale are found on the trunk and extremities. The lesions can become vesicular, hemorrhagic, crusted, or superinfected. By 2 to 6 weeks these lesions become flat and hyper- or hypopigmented. The lack of the herald patch and the chronicity of the lesions can help distinguish it from pityriasis rosea. Treatment is with lubricants and occasionally topical steroids, and in some children, treatment with erythromycin has hastened its resolution.

Other conditions included in the differential are drug eruptions and viral exanthems. A thorough history might elucidate any medications that are causing a drug eruption, and findings of symptoms related to a viral infection would help assist the diagnosis of a viral exanthema.

## COMPREHENSION QUESTIONS

- 33.1 A 4-year-old boy is dismissed from his day care for a rash and comes to the clinic for evaluation. The “rash” is a 2-cm circle on his left cheek that is erythematous, scaly, and has a discrete and raised border. The skin in the middle of the lesion seems unaffected; he scratches it occasionally. He is otherwise healthy and has no serious medical history. His rash is most likely:
- A. Nummular eczema
  - B. Tinea corporis
  - C. Pityriasis rosea
  - D. Burn
  - E. Psoriasis
- 33.2 A 7-year-old boy, otherwise healthy, presents with 2 weeks of several hypopigmented patches on his face. They are not pruritic, but do seem to have a fine scale. There is no erythema, no crusting, no raised border, and no tenderness. The borders of the hypopigmentation are not sharply demarcated, and there is no other hypopigmentation noted. The most likely diagnosis for this patient is:
- A. Atopic dermatitis

- B. Vitiligo
- C. Tinea corporis
- D. Pityriasis alba
- E. Nickel dermatitis

33.3 A 15-year-old girl presents to the clinic for evaluation of a rash. She is concerned about a pruritic erythematous lichenified patch below her umbilicus that has waxed and waned for several years. Recently, however, she also developed a similar rash above her umbilicus near the site of a recent piercing. She wonders if the piercing studio didn't do a good job cleaning their equipment. Her skin condition is most likely:

- A. Atopic dermatitis
- B. Intertrigo
- C. Tinea corporis
- D. Seborrheic dermatitis
- E. Nickel allergy

33.4 You are asked to consult on a 9-month-old fully immunized infant admitted to the hospital for his third episode of lobar pneumonia. A review of his past history also reveals several episodes of impetigo and otitis media, a chronic diagnosis of atopic dermatitis that has been difficult to control, and a mention of easy bruising. The review of systems identifies occasional oral bleeding after brushing his two new teeth. Laboratory studies show a platelet count of 60,000 platelets/mm<sup>3</sup>. The most likely diagnosis in this case is:

- A. Thrombocytopenia with absent radius (TAR) syndrome
- B. Wiskott-Aldrich syndrome (WAS)
- C. Idiopathic thrombocytopenic purpura (ITP)
- D. Thrombotic thrombocytopenic purpura (TTP)
- E. Lichen simplex chronicus

## ANSWERS



- 33.1 B.** Tinea corporis (also known as “ringworm” describing its characteristic skin finding) is a superficial cutaneous fungal infection caused primarily by *Microsporum canis*, *Trichophyton tonsurans*, *T. rubrum*, and *T. mentagrophytes*. The lesion typically starts as an erythematous papule that expands to form a circular, scaly, and erythematous lesion with raised borders. As the lesions get larger, they may develop central clearing. Pruritus is not a universal symptom. Treatment is with topical azoles (eg, ketoconazole, clotrimazole) or systemic antifungals (such as griseofulvin) in more diffuse cases. Pityriasis rosea (PR) and nummular eczema are both in the differential as they can cause circular skin lesions. Patients with PR go on to develop multiple lesions on the trunk in a characteristic pattern, making the clinical distinction clear. Lesions of nummular eczema are discrete, circular, and pruritic; central clearing is not typical.
- 33.2 D.** Pityriasis alba is a common condition in children, manifest by hypopigmented macules with a fine scale, typically found on the face, neck, upper trunk, and proximal upper extremities. Pruritus is usually absent. These lesions are benign, and thought to be a manifestation of dry skin. The lesions are more prominent in dark-skinned individuals, as well as after sun exposure when the surrounding skin darkens and the affected area does not. The borders are not sharply demarcated, distinguishing the lesions from vitiligo. Tinea corporis (ringworm) lesions typically have raised erythematous borders with central clearing. Nickel dermatitis is seen in areas of skin exposed to nickel (under the umbilicus or on the earlobes in pierced individuals). Atopic dermatitis, as described in the initial case, is erythematous, scaly, and pruritic. Treatment of pityriasis alba is skin hydration, and low-dose topical corticosteroids may be used for itching. It is important to inform the patient and family that repigmentation may take months.
- 33.3 E.** Nickel contact dermatitis is seen in areas exposed to nickel, such as the area of skin below the umbilicus that is in contact with the back of snaps and buttons on pants; the neck, in children wearing a necklace; behind the ears, in those wearing glasses; and any site associated with piercing. Affected individuals can avoid inexpensive pierced jewelry and choose instead jewelry with surgical steel posts. The back of pants snaps may be painted with nail polish, thereby preventing skin contact

with the offending metal. The location in the vignette is not typical of intertrigo, found in areas of skin apposition.

**33.4 B.** This patient has Wiskott-Aldrich syndrome (WAS), a rare X-linked disorder characterized by recurrent bacterial infections, bleeding secondary to thrombocytopenia in addition to platelet dysfunction, and chronic dermatitis. The skin findings are identical to atopic dermatitis. Platelet counts usually are between 1000 and 80,000 platelets/mm<sup>3</sup>, and the platelets are small and dysfunctional. Autoimmune hemolytic anemia occurs in about a third of these patients. The disorder is progressive; without marrow transplantation, most patients die by the age of 3 years. Patients transplanted before the age of 5 have a 71% (matched unrelated donor) to 87% (matched sibling donor) survival rate. TTP is a thrombotic microangiopathy more common in adults, ITP is an isolated thrombocytopenia, and TAR is characterized by the absence of the radius in the forearm and thrombocytopenia; none of these conditions are characterized by the immune dysfunction or the chronic dermatitis seen in the vignette. Lichen simplex chronicus is a chronic localized dermatitis with round or oval lichenified patches; while these lesions may look similar to those described in the clinical vignette of this question, the exposure history makes the diagnosis clear.

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### CLINICAL PEARLS

- ▶ Pityriasis rosea is a common eruption in childhood associated with a herald patch.
  - ▶ The lesions of pityriasis rosea align along cutaneous cleavage planes resulting in a “Christmas tree” pattern.
  - ▶ An important diagnosis in the differential of pityriasis rosea is secondary syphilis.
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## CASE 34

A 16-year-old adolescent male resident at the local police department's boot camp was in his normal state of health until this morning, when he developed a headache and a fever of 105.8°F (41°C). Over the next 2 hours, he developed a stiff neck and began vomiting. He was brought to the emergency department (ED) when he developed altered mental status. No one else in the facility is ill. In the ED, his heart rate is 135 bpm, blood pressure 120/70 mm Hg, respiratory rate 25 breaths/min, and temperature 104°F (40°C). He is combative, unaware of his surroundings, and does not follow instructions. Kernig and Brudzinski signs are present.

- ▶ What is the most likely diagnosis?
- ▶ How would you confirm the diagnosis?
- ▶ What treatment is indicated?
- ▶ What are possible complications?

### ANSWERS TO CASE 34: **Bacterial Meningitis**

*Summary:* A 16-year-old adolescent boy has fever, headache, stiff neck, and altered mental status. He is tachycardic but normotensive.

- **Most likely diagnosis:** Bacterial meningitis
- **Confirm diagnosis:** Lumbar puncture (LP)

- **Treatment:** Intravenous antibiotics
- **Complications:** Deafness, cranial nerve palsies, and, rarely, hemiparesis or global brain injury.

## ANALYSIS

### *Objectives*

1. Describe the typical presentation of bacterial meningitis.
2. Describe how a patient's age affects the presentation and outcome of bacterial meningitis.
3. List typical pathogens and appropriate treatment strategies by age group.

### *Considerations*

This teen has the typical triad of meningitis symptoms: fever, headache, and a stiff neck; his altered mental status is another often-seen finding. Other causes of mental status changes include viral meningoencephalitis, trauma, intentional or accidental ingestion, and hypoglycemia. Of these alternatives, only viral meningoencephalitis would likely explain the fever and stiff neck.

### APPROACH TO:

#### **Bacterial Meningitis**

## DEFINITIONS

**BRUDZINSKI SIGN:** A physical finding consistent with meningitis; while the patient is supine, the neck is passively flexed resulting in involuntary knee and hip flexion.

**ENCEPHALITIS:** Brain parenchyma inflammation causing brain dysfunction.

**KERNIG SIGN:** A physical finding consistent with meningitis; while the patient is supine, the legs are flexed at the hip and knee at 90° angle resulting in pain with leg extension.

**MENINGITIS:** Leptomeningeal inflammations, typically infectious, but may also be caused by foreign substances.

# CLINICAL APPROACH

The microbiology and clinical presentation of meningitis vary based on the patient's age. The incidence of **neonatal meningitis** is between 0.2 and 0.5 cases per 1000 live births, most commonly due to *Escherichia coli* and **group B *Streptococcus*** (*Streptococcus agalactiae*). *Listeria monocytogenes* and other organisms (*Citrobacter* sp, *Staphylococcus* sp, group D streptococci, and *Candida* sp) are less common. Infants at increased risk for meningitis include low-birth-weight and preterm infants, and those born to mothers with chorioamnionitis, after a prolonged rupture of the amniotic membranes, or by traumatic delivery. Most neonatal bacterial meningitis occurs by hematogenous spread. Clinical symptoms in infants are nonspecific and not the typical triad of headache, fever, and stiff neck; instead, infants may have thermal instability (often hypothermia), poor feeding, emesis, seizures, irritability, and apnea. Infants may have a bulging fontanelle, and they demonstrate generalized hyper- or hypotonicity.

**Bacterial meningitis in older children** is usually caused by *Streptococcus pneumoniae* or *Neisseria meningitidis*; vaccination has essentially eliminated *Haemophilus influenzae* type B. Other rarer causes in this age group include *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Salmonella* sp, and *Listeria monocytogenes*.

The incidence of pneumococcal meningitis is 1 to 6 cases per 100,000 children per year, more commonly occurring in the winter. It is an **encapsulated pathogen**; children with a **poorly functioning or absent spleen are at higher risk**. Children with **sickle cell disease** have an infection incidence 300 times greater than in unaffected children. Other risk factors include sinusitis, otitis media, pneumonia, and head trauma with subsequent cerebrospinal fluid (CSF) leak.

*Neisseria meningitidis* colonizes the upper respiratory tract in approximately 15% of normal individuals; carriage rates up to 30% are seen during invasive disease outbreaks. Disease appears to be caused by “new” infection rather than long-term carriage. In the United States, most disease is caused by serotypes B and C. Family members and day care workers in close contact with children having meningitis are at 100- to 1000-fold increased risk for contracting disease. A plethora of other bacterial, viral, fungal, and mycobacterial agents can cause meningitis.

The classic symptoms of meningitis seen in older children and adults may be accompanied by mental status changes, nausea, vomiting, lethargy, restlessness, ataxia, back pain, Kernig and Brudzinski signs, and cranial nerve palsies. Approximately one-quarter to one-third of patients have a seizure during the illness course. Patients with *N meningitidis* can have a petechial or purpuric rash (purpura fulminans), which is associated with septicemia. Patients with septicemia due to *N meningitidis* often are gravely ill and may or may not have associated meningitis.

The test of choice for suspected meningitis is an LP, which usually can be performed safely in children with few complications.

Contraindications include a skin infection over the planned puncture site, evidence of or clinical concern for increased intracranial pressure, and a critically ill patient who may not tolerate the procedure. Cerebrospinal fluid analysis includes Gram stain and culture, white and red blood cell counts, and protein and glucose analysis. Bacterial antigen screens can be performed in patients already receiving antibiotics before the LP; these antigens may persist for several days, even when the culture is negative. Typical bacterial meningitis findings include an elevated opening pressure, several hundred to thousands of white blood cells with polymorphonuclear cell predominance, and elevated protein and decreased glucose levels.

Treatment strategies vary by patient age, likely pathogens, and local resistance patterns. A CSF Gram stain can guide the decision-making process. In the neonatal period, ampicillin often is combined with a third-generation cephalosporin or an aminoglycoside to cover infections caused by group B *Streptococcus*, *L monocytogenes*, and *E coli*. Neonates in an intensive care unit may be exposed to nosocomial infections; prevalent pathogens in that nursery must be considered.

In some locales, more than half of the pneumococcal isolates are intermediately or highly penicillin resistant; 5% to 10% of the organisms are cephalosporin resistant. Thus, in suspected pneumococcal meningitis, a third-generation cephalosporin combined with vancomycin is often recommended. Most *N meningitidis* strains are susceptible to penicillin or cephalosporins.

Acute meningitis complications may include seizures, cranial nerve palsies, cerebral infarction, cerebral or cerebellar herniation, venous sinus thrombosis, subdural effusions, syndrome of inappropriate (secretion)

of antidiuretic hormone (SIADH) with hyponatremia, and central diabetes insipidus. The **most common long-term sequela is hearing loss** (up to 30% of patients with pneumococcus); patients with bacterial meningitis usually have a hearing evaluation at the conclusion of antibiotic treatment. Mental retardation, neuropsychiatric and learning problems, epilepsy, behavioral problems, vision loss, and hydrocephalus are less commonly seen.

## COMPREHENSION QUESTIONS

- 34.1 A 13-year-old boy has a 1-day history of fever and lethargy, and was unable to be awoken this morning. In the emergency department his respiratory rate is 7 breaths/min, heart rate 55 bpm, temperature 105.8°F (41°C), and blood pressure (BP) 60/40 mm Hg. He has altered mental status, a stiff neck, and a purpuric rash over his trunk. Which of the following is the most appropriate next step in the management of this patient?
- A. Computed tomography of the head
  - B. Intravenous antibiotics
  - C. Intubation
  - D. Lumbar puncture
  - E. Serum chemistries
- 34.2 An 8-year-old girl has persistent fever and headaches. Her parents report that for the 2 weeks prior she has complained of frontal headache that was significant enough to keep her away from school. She has had intermittent temperature elevations to 101°F (38.3°C), and she started vomiting a nonbloody, nonbilious fluid a few days ago. She has had frequent otitis media and sinusitis episodes, but her last episode of otitis media occurred approximately 5 weeks ago. On examination, you find a lethargic girl in no respiratory distress. She has a temperature of 100°F (37.7°C), heart rate 109 bpm, and blood pressure (BP) 100/60 mm Hg. She has nuchal rigidity and frontal sinus tenderness. Which of the following is the most appropriate next step in the management of this patient?
- A. Computed tomography of the head
  - B. Intravenous promethazine for emesis
  - C. Lumbar puncture
  - D. Sinus radiographs
  - E. Trial of subcutaneous sumatriptan for migraine



- 34.3 A 2-week-old infant develops a temperature to 102°F (38.9°C). Pregnancy and delivery were uncomplicated. The irritable, fussy infant has a heart rate of 170 bpm and respiratory rate 40 breaths/min. The anterior fontanelle is full, but he has no nuchal rigidity; the rest of the examination is unremarkable. Which of the following is the most appropriate management of this infant?
- A. Encourage oral fluids and office follow-up in 24 hours.
  - B. Order computed tomography of the head followed by an LP.
  - C. Perform an LP, blood culture, and urine culture, and admit to the hospital.
  - D. Prescribe intramuscular ceftriaxone and clinic follow-up in 1 week.
  - E. Prescribe oral amoxicillin and clinic follow-up in 1 week.
- 34.4 A 14-year-old boy complains of fever and stiff neck for 2 days. He has a sore throat and has been unable to eat for a day because of the pain. On examination, he is alert and oriented, but he has nuchal rigidity and posterior pharyngeal midline fullness. He drools to avoid the pain of swallowing. Which of the following is the best next step in the management of this patient?
- A. Order computed tomography of the head.
  - B. Order lateral neck radiographs.
  - C. Perform a lumbar puncture.
  - D. Prescribe intramuscular antibiotics.
  - E. Prescribe oral antibiotics.

## ANSWERS

- 34.1 C. This patient in the question has meningococcemia; he is in shock, and he is about to die. The **ABCs** of Airway, Breathing, and Circulation should always take precedence over diagnostic studies. *N meningitidis* can present as meningococcemia with purpura and shock; in some cases patients will also have meningitis. The LP should be deferred, however, until he is clinically stable. Intravenous fluids through

a large-bore catheter to support his cardiovascular status and antibiotics should be administered immediately after stabilization of his airway.

- 34.2 A. This girl's history of sinusitis and a prolonged headache with worsening emesis and nuchal rigidity suggest an intracranial abscess due to her sinusitis. In her case, CNS imaging (with contrast) is performed prior to an LP. Performing an LP when a mass lesion might be causing increased intracranial pressure can result in herniation of the brain and patient death. Sinus films would show sinusitis but would not reveal an intracranial abscess. Merely treating her symptoms with promethazine or sumatriptan would delay the diagnosis of her underlying problem.
- 34.3 C. This infant potentially has a serious bacterial infection, and an evaluation including an LP is performed. Infants do not reliably demonstrate a Kernig or Brudzinski sign; a lack of nuchal rigidity should not preclude an LP. Computed tomography scan before an LP in an infant with an open anterior fontanelle is rarely necessary, as brain herniation is exceedingly rare. A course of oral antibiotics, or a single dose of ceftriaxone, is not sufficient to treat meningitis or septicemia.
- 34.4 B. A retropharyngeal abscess is causing this boy's neck stiffness; he does not have meningitis. He has a normal mental status, dysphagia, and fullness in his oropharynx. Lateral neck films are a simple way to confirm this diagnosis. Prescribing antibiotics without identifying the diagnosis would not be appropriate in this case.
- 

## CLINICAL PEARLS

- ▶ The typical meningitis presentation in older children consists of fever, headache, and nuchal rigidity.
- ▶ Nuchal rigidity is not a reliable finding of meningitis until 12 to 18 months of age.
- ▶ Pneumococcal disease (including meningitis) is more common in patients with functional or anatomic asplenia.
- ▶ Approximately one-third of meningitis patients have a seizure at some point in the disease.
- ▶ Typical cerebrospinal fluid findings of bacterial meningitis include elevated protein level, reduced glucose concentration, and several hundred to thousands of white blood cells per cubic millimeter.

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### CASE 35

You receive a call from the mother of a previously healthy 2-year-old boy. Yesterday, he developed a temperature of 104°F (40°C), cramping abdominal pain, emesis, and frequent watery stools. The mother assumed he had the same gastroenteritis like his aunt and many other children in his day care center.

However, today he developed bloody stools with mucus and seemed more irritable. While you are asking about his current hydration status, the mother reports that he is having a seizure. You tell her to call the ambulance and then notify the local hospital's emergency center of his imminent arrival.

- ▶ What is the most likely diagnosis?
- ▶ How can you confirm this diagnosis?
- ▶ What is the best management for this illness?
- ▶ What is the expected course of this illness?

### ANSWERS TO CASE 35: **Bacterial Enteritis**

*Summary:* This child was exposed in his day care center and at home to gastrointestinal (GI) illnesses. He has fever, abdominal pain, and watery diarrhea that progressed to bloody diarrhea with mucus. He had a new-onset seizure.

- **Most likely diagnosis:** Bacterial enteritis with neurologic manifestations.
- **Diagnostic tools:** Fecal leukocytes, fecal blood, and stool culture.
- **Management:** Varies with age and suspected organism; hydration and electrolyte correction is a priority. *Salmonella* infections are self-limited and generally are not treated except in patients younger than 3 months or in immunocompromised individuals; *Shigella* infections, although self-limited, are generally treated to shorten the illness and decrease organism excretion. Antimotility agents are not used.
- **Course:** Left untreated, most GI infections in healthy children will spontaneously resolve. Extraintestinal infections are more likely in immunocompromised individuals.

## ANALYSIS

### *Objectives*

1. Describe the typical clinical presentation of bacterial enteritis.
2. List potential pathogens for gastroenteritis, considering the patient's age.

3. Discuss treatment options and explain when treatment is necessary.
4. Discuss potential complications of bacterial enteritis.

### ***Considerations***

Bloody stools can be caused by many diseases, not all of which are infectious. In this child, GI bleeding also could be caused by Meckel diverticulum, intussusception, Henoch-Schönlein purpura, hemolytic-uremic syndrome, *Clostridium difficile* colitis, and polyps. The description is most consistent, however, with infectious enteritis typical of *Shigella* or *Salmonella*.

APPROACH TO:

**Bacterial Enteritis**

## **DEFINITIONS**

**COLITIS:** Inflammation of the colon.

**DIARRHEA:** Frequent passage of unusually soft or watery stools.

**DYSENTERY:** An intestinal infection resulting in severe bloody diarrhea with mucus.

**ENTERITIS:** Inflammation of the small intestine, usually resulting in diarrhea; may be a result of infection, immune response, or other causes.

## **CLINICAL APPROACH**

***Salmonella* organisms** are aerobic gram-negative rods and can survive as facultative anaerobes. They are motile and do not ferment lactose. Infection is **more common in warmer months**. *Salmonella* infections can be separated into nontyphoidal disease (gastroenteritis, meningitis, osteomyelitis, and bacteremia) and typhoid (or enteric) fever, caused primarily by *Salmonella typhi*. Outbreaks usually occur sporadically but can be food related and occur in clusters. Many animals harbor ***Salmonella***. Exposure to **poultry and raw eggs probably is the most common source of human infection**; sources may also include iguanas and turtles. Infection requires the ingestion of many organisms; person-to-person spread is uncommon.

Gastroenteritis is the most common nontyphoidal disease presentation of *Salmonella*. Children usually have sudden onset of nausea, emesis, cramping abdominal pain, and watery or bloody diarrhea. Most develop a low-grade fever; some have **neurologic symptoms** (confusion, headache, drowsiness, and seizures). Between 1% and 5% of patients with *Salmonella* infection develop transient bacteremia, with subsequent extraintestinal infections (osteomyelitis, pneumonia, meningitis, and arthritis); these findings are more common in immunocompromised patients and in infants.

***Shigella* organisms are small gram-negative bacilli.** They are non-lactose fermenting facultative anaerobes, and have recently been shown to be motile. Four *Shigella* species cause human disease: *S dysenteriae*, *S boydii*, *S flexneri*, and *S sonnei*. Infections most commonly occur in warmer months and in the first 10 years of life (peaking in the second and third years). Infection usually is transmitted **person to person** but may occur through food and water. Relatively few *Shigella* organisms are required to cause disease. Typically, children have fever, cramping abdominal pain, watery diarrhea (often progressing to small bloody stools), and anorexia; they appear ill. Untreated, diarrhea typically lasts 1 to 2 weeks and then resolves. **Neurologic findings** may include headache, confusion, seizure, or hallucinations. *Shigella* meningitis is infrequent. Uncommon complications include rectal prolapse, cholestatic hepatitis, arthritis, conjunctivitis, and cystitis. Rarely, *Shigella* causes a rapidly progressive sepsis-like presentation (Ekiri syndrome) that quickly results in death.

*Salmonella* or *Shigella* tests include a **stool culture**, although results frequently are negative even in infected test subjects. **Fecal leukocytes usually are positive**, but this nonspecific finding only suggests colonic inflammation. An occult blood assay often is positive. In ***Shigella* infection**, the peripheral white count usually is normal, but a **remarkable left shift** often is seen with more bands than polymorphonuclear cells. *Salmonella* infection usually results in a mild leukocytosis.

**Treatment focuses on fluid and electrolyte balance correction.** **Antibiotic treatment of *Salmonella* usually is not necessary**; it does not shorten the GI disease course and **may increase the risk of hemolytic-uremic syndrome (HUS)**. Infants younger than 3 months of age and immunocompromised individuals often are treated for GI infection, as they are at increased risk for disseminated disease. *Shigella* is self-limited as well,

but antibiotics shorten the illness course and decrease the duration organisms are shed. Antimotility agents are not indicated for either *Salmonella* or *Shigella*.

In addition to the above organisms, enteroinvasive *Escherichia coli*, *Campylobacter* sp, and *Yersinia enterocolitica* can cause dysentery, with fever, abdominal cramps, and bloody diarrhea. *Yersinia* can cause an “acute abdomen” picture. Enterohemorrhagic (or Shiga toxin-producing) *E coli* can cause bloody diarrhea but usually no fever. Infection with *Vibrio cholera* produces vomiting and profuse, watery, nonbloody diarrhea with little or no fever.

**Hemolytic-uremic syndrome, the most common cause of acute childhood renal failure, develops in 5% to 8% of children with diarrhea caused by enterohemorrhagic *E coli* (O157:H7);** it is seen less commonly after *Shigella*, *Salmonella*, and *Yersinia* infections. It usually is seen in children younger than 4 years. The underlying process may be microthrombi, microvascular endothelial cell injury causing microangiopathic hemolytic anemia, and consumptive thrombocytopenia. Renal glomerular deposition of an unidentified material leads to capillary wall thickening and subsequent lumen narrowing. The typical presentation occurs 1 to 2 weeks after a diarrheal illness, with acute onset of pallor, irritability, decreased or absent urine output, and even stroke; children may also develop petechiae and edema. Treatment is supportive; some children require dialysis. Most children recover and regain normal renal function; all are followed after infection for hypertension and chronic renal failure.

## COMPREHENSION QUESTIONS

35.1 A 2-year-old boy developed emesis and intermittent abdominal pain yesterday, with several small partially formed stools. His parents were not overly concerned because he seemed fine between the pain episodes. Today, however, he has persistent bilious emesis and has had several bloody stools. Examination reveals a lethargic child in mild distress; he is tachycardic and febrile. He has a diffusely tender abdomen with a vague tubular mass in the right upper quadrant. Which of the following is the most appropriate next step in managing this condition?

A. Computed tomography of the abdomen

- B. Air contrast enema
- C. Intravenous antibiotics for *Shigella*
- D. Parental reassurance
- E. Stool cultures

35.2 A previously healthy 2-year-old girl had 3 days of bloody diarrhea the previous week that spontaneously resolved. Her mother now thinks she looks pale. On examination, you see that she is afebrile, her heart rate is 150 bpm, and her blood pressure is 150/80 mm Hg. She is pale and irritable, has lower-extremity pitting edemas, and has scattered petechiae. After appropriate laboratory studies, initial management should include which of the following?

- A. Careful management of fluid and electrolyte balance
- B. Contrast upper GI series with small bowel delay films
- C. Intravenous antibiotics and platelet transfusion
- D. Intravenous steroids and aggressive fluid resuscitation
- E. Intubation and mechanical ventilation

35.3 A family reunion picnic went awry when the majority of attendees developed emesis and watery diarrhea with streaks of blood. Unaffected attendees did not eat the potato salad. A few ill family members are mildly febrile. They come as a group to your clinic, seeking medications. Which of the following is the most appropriate management for their condition?

- A. Antimotility medication
- B. Hydration and careful follow-up
- C. Intramuscular ceftriaxone
- D. Oral amoxicillin
- E. Oral metronidazole

35.4 You are asked to see a 1-month-old infant to provide a second opinion. During a brief, self-limited, and untreated diarrheal episode the previous week, his primary physician ordered a stool assay for *Clostridium difficile* toxin; the result is positive. The infant now is completely asymptomatic, active, smiling, and well hydrated. His physician said



treatment was not necessary, but the mother wants treatment. Which of the following is the most appropriate response?

- A. *Clostridium difficile* commonly colonizes the intestine of infants; treatment without symptoms is not warranted.
- B. The infant should take a 7-day course of oral metronidazole.
- C. The infant should take a 10-day course of oral vancomycin.
- D. The infant should be admitted to the hospital for intravenous metronidazole
- E. A repeat study to look for the *C difficile* organism is warranted.

## ANSWERS

- 35.1 **B.** This child has an intussusception. He has bloody stools, but he also has bilious emesis, colicky abdominal pain, and a right upper quadrant mass. In experienced hands, an air contrast enema procedure may be diagnostic and therapeutic. Ensure that a surgeon and a prepared operating room are available should the reduction through contrast enema fail or result in intestinal perforation. While a CT scan may diagnose intussusception, an enema is preferred as it can be therapeutic as well as diagnostic.
- 35.2 **A.** Hemolytic-uremic syndrome may be seen after bloody diarrhea, presenting with anemia, thrombocytopenia, and nephropathy. The child in question is hypertensive and has edema, so large amounts of fluids may be counterproductive. Steroids typically are not helpful. The thrombocytopenia is consumptive; unless the patient is actively bleeding, platelet transfusion is not helpful. Most of the care for such patients is supportive, concentrating on fluids and electrolytes. Early dialysis may be needed. Hypertensive patients should have appropriate control of their blood pressure.
- 35.3 **B.** This family probably has *Salmonella* food poisoning. Antibiotics are not indicated for this healthy family, and antimotility agents may prolong the illness. Frequent handwashing should be emphasized.
- 35.4 **A.** *Clostridium difficile* colonizes approximately half of normal healthy infants in the first 12 months. In this infant without a history of antibiotic

treatment or current symptoms, treatment is unnecessary. *C difficile* colitis rarely occurs without a history of recent antibiotic use.

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## CLINICAL PEARLS

- ▶ In normal children older than 3 months, isolated intestinal *Salmonella* infections do not require antibiotic treatment; antibiotics do not shorten the course of illness.
  - ▶ Suspected *Shigella* intestinal infections usually are treated to shorten the illness course and to decrease organism shedding.
  - ▶ Hemolytic-uremic syndrome, a potential sequela of bacterial enteritis, is the most common cause of acute renal failure in children.
- 

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## CASE 36

A 15-year-old adolescent female has periumbilical pain that began 8 hours ago; since then she has vomited once and has had one small, loose bowel movement. Her last meal was 12 hours ago, and she is not hungry. She denies dysuria, urinary frequency, and sexual activity; her last menses a week ago was normal. On examination, she is moderately uncomfortable, mildly tachycardic, and has a low-grade fever of 101.5°F (38.6°C). Her abdominal examination reveals few bowel sounds, rectus muscle rigidity, and tenderness to palpation, particularly periumbilically. Breath sounds are clear; she has no rashes. Her pelvic examination shows no vaginal discharge, but there is some abdominal tenderness with gentle bimanual palpation. She has right lower quadrant pain with digital rectal examination.

- What is the most likely diagnosis?
- What is the next step in the management of this patient?

## ANSWERS TO CASE 36: **Appendicitis**

*Summary:* A 15-year-old adolescent female with periumbilical pain of 8-hour duration, followed by anorexia, emesis, and a loose bowel movement. She

has no dysuria or sexual activity, and the pain appears unrelated to her menses. Her physical examination shows a quiet, rigid, tender abdomen, and pain with digital rectal examination.

- **Most likely diagnosis:** Appendicitis
- **Next step in management:** A surgeon should be consulted once the diagnosis of appendicitis is suspected. Abdominal ultrasound has high sensitivity for diagnosis of appendicitis in experienced pediatric centers, but abdominal computed tomography (CT) is more generally used. Urinalysis is useful to eliminate a urinary tract infection (UTI) as a cause, and a complete blood count (CBC) often shows leukocytosis. Despite this adolescent's denial of sexual activity, a urine pregnancy test should be obtained.

## ANALYSIS

### *Objectives*

1. Recognize the presenting clinical signs for appendicitis.
2. Know the differential diagnosis for appendicitis.
3. Recognize the need to maintain a high index of suspicion for appendicitis to prevent possible complications.

### *Considerations*

The definitive diagnosis of appendicitis may not be made until surgery. For this patient, the initial **abdominal pain followed by anorexia and vomitings** suggests appendicitis. **The pain of appendicitis classically begins periumbilically and then migrates to the right lower quadrant.** The pain can occur laterally (retrocecal appendix), or it can be more diffuse (perforated appendix with resultant generalized peritonitis). The utility of rectal examinations for children with suspected appendicitis is debatable; they can be helpful for localizing the pain source in a female adolescent.

The adolescent female in this case is early in her disease process and arguably might be safely observed for a few hours if the diagnosis remains in question. However, once appendicitis seems likely, surgical management should occur in a timely fashion; perforation rates exceed 65% if diagnosis is

delayed beyond 36 to 48 hours from symptom onset. Complications, such as wound infection, abscess formation, intestinal obstruction, or adhesions, are infrequent (5%-10%) following uncomplicated appendectomy but increase (15%-30%) with appendiceal perforation.

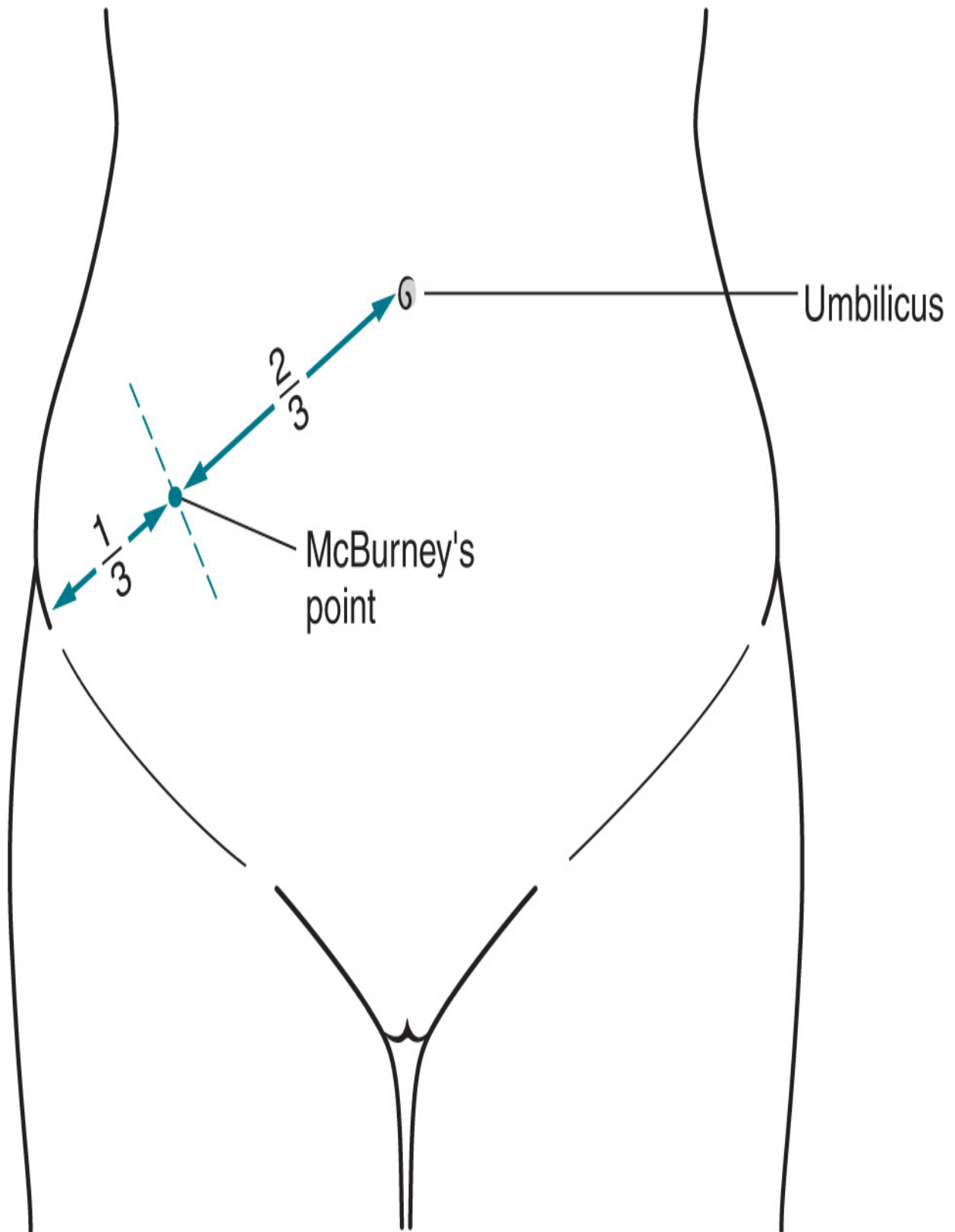
APPROACH TO:

**Appendicitis**

## DEFINITIONS

**APPENDICITIS:** Appendix inflammation occurs after luminal obstruction. If the appendix is not removed, appendiceal wall necrosis results in perforation and peritoneal contamination.

**MCBURNEY'S POINT:** The junction of the lateral and middle third of the line joining the right anterior superior iliac spine and the umbilicus ([Figure 36-1](#)); typically this area is of greatest discomfort in acute appendicitis.



**Figure 36-1.** McBurney's point.

**PSOAS SIGN:** Irritation of the psoas muscle caused by active right thigh flexion or passive right hip extension in patients with appendicitis.

**OBTURATOR SIGN:** Irritation of the obturator muscle caused by passive internal rotation of the right thigh in patients with appendicitis.

**ROVSING'S SIGN:** Palpation of the left lower quadrant causes pain at the right lower quadrant in patients with appendicitis.

## CLINICAL APPROACH

A person's lifetime risk of appendicitis has been estimated at 6% to 20%, with the peak incidence in adolescence. Intrinsic appendiceal obstruction caused by inspissated fecal material (an appendicolith) is found in 30% to 50% of patients at the time of surgery. Extrinsic compression usually is caused by enlarged lymph nodes associated with bacterial or viral infections. The obstruction causes vascular thrombosis, ischemia, and, ultimately, perforation.

The differential diagnosis for acute abdominal pain in childhood is long ([Table 36-1](#)). Worsening abdominal pain in the periumbilical area, which then migrates to the right lower quadrant, is characteristic of acute appendicitis. Likewise, anorexia, nausea, and vomiting that begin after the onset of pain is strongly indicative of the diagnosis.

Condition	Signs and Symptoms
Appendicitis	Right lower quadrant pain, abdominal guarding, and rebound tenderness
Bacterial enterocolitis	Diarrhea (may be bloody), fever, vomiting
Cholecystitis	Right upper quadrant pain, often radiating to subscapular region of the back
Constipation	Infrequent, hard stools, and recurrent abdominal pain; sometimes enuresis
Diabetic ketoacidosis	History of polydipsia, polyuria, and weight loss
Ectopic pregnancy	Lower abdominal pain, vaginal bleeding, and an abnormal menstrual history
Gastroenteritis	Fever, vomiting, and hyperactive bowel sounds



Hemolytic-uremic syndrome	Irritability, pallor, bloody diarrhea, anemia, thrombocytopenia, decreased urine output, hypertension
Henoch-Schönlein purpura	Purpuric lesions, especially of lower extremities and joint pain, blood in stool (guaiac positive)
Hepatitis	Right upper quadrant pain and jaundice
Inflammatory bowel disease	Weight loss, diarrhea, and malaise
Mittelschmerz	Sudden onset of right or left lower quadrant pain with ovulation, may have copious mucoid vaginal discharge
Nephrolithiasis	Hematuria, colicky abdominal pain
Ovarian cyst	Acute pain with rupture or torsion; possible hypotension and fainting accompany hemorrhage in the peritoneum

Pancreatitis	(Severe, boring) mid-epigastric abdominal pain that might radiate to the back or worsen with eating, persistent vomiting, elevated amylase and lipase
Pelvic inflammatory disease	Cervical motion tenderness; white blood cells in the vaginal secretions
Pneumonia	Fever, cough, and crackles on auscultation of the chest
Sickle cell crisis	Anemia and extremity pain
Streptococcal pharyngitis	Fever, sore throat, and headache
Urinary tract infection	Dysuria, fever, vomiting, flank pain, pyuria, urine nitrites

**Table 36-1 • PARTIAL DIFFERENTIAL DIAGNOSIS OF ACUTE ABDOMINAL PAIN IN CHILDREN BEYOND INFANCY**

A gentle abdominal examination can provide meaningful data while not frightening the child. Observation of the child getting on and off the examination table can be revealing; children with appendicitis avoid sudden movements (such as jumping off the table). The abdomen is inspected, then auscultated for bowel sounds, followed by gentle palpation for the area of maximal tenderness and rigidity. Gentle finger percussion assesses for peritoneal irritation (“rebound tenderness”). If performed, a rectal examination should occur last.

Although not a specific finding, **leukocytosis with a predominance of polymorphonuclear cells (a “left shift”) on a CBC supports an inflammatory process.** Hematuria and pyuria raise the possibility of a genitourinary etiology, but they can occur with acute appendicitis if it also causes irritation of the bladder or ureteral wall. Plain abdominal radiographs

can be obtained but are infrequently helpful. Psoas shadow obliteration, right lower quadrant intestinal dilatation, scoliosis toward the affected region, and an appendicolith (seen in 10% of cases) support appendicitis. Chest radiographs eliminate pneumonia as an alternate diagnosis. **Ultrasonography is more sensitive than plain films for appendicitis and is particularly useful in female adolescents**, in whom the differential diagnosis includes ovarian cysts and pregnancy. Its main limitation is that the appendix cannot always be visualized. **CT** has become the diagnostic test of choice in most centers and is particularly helpful for patients who are **neurologically impaired, immunologically suppressed, or obese**, or for patients in whom **perforation** is suspected. Its disadvantages are the amount of radiation exposure generated and increased cost, and that it may give limited information without the use of contrast.

**Definitive treatment is surgical removal of the appendix (appendectomy)**, accomplished as soon as the diagnosis is strongly suspected to prevent perforation (if it has not already occurred). For perforated appendicitis, initial management consists of intravenous antibiotics and fluid replacement; its course may be complicated by sepsis, abscess formation, or prolonged (4-5 days) paralytic ileus. Percutaneous drainage catheters can be used to drain the abscess and then appendectomy is performed at a later time.

## COMPREHENSION QUESTIONS

- 36.1 A 7-year-old has right-sided abdominal pain and fever to 102°F (38.9°C). His mother says that he has had 2 days of poor appetite and cough; he had two loose stools earlier in the day. On examination, his temperature is 101.7°F (38.7°C), his heart rate is 120 bpm, and his respiratory rate is 50 breaths/min. Breath sounds are diminished, and the abdomen is diffusely tense with hypoactive bowel sounds. Which of the following would likely lead to the diagnosis?
- A. Abdominal computed tomography
  - B. Chest radiograph
  - C. Liver function tests
  - D. Stool leukocytes
  - E. Stool for culture, ova, and parasites

36.2 A 14-year-old adolescent female with a 3-day history of abdominal pain, anorexia, and vomiting and a 1-day history of fever underwent laparoscopic surgery for suspected appendicitis, which was perforated at the time of surgery. Intravenous ampicillin, gentamicin, and clindamycin were initiated prior to surgery and continued postoperatively. On the seventh postoperative day, she continues to have fevers to 102°F (38.9°C). Which of the following is the next most appropriate step in management?

- A. Add metronidazole to the antibiotic regimen.
- B. Change the antibiotics to amikacin and a cephalosporin.
- C. Order a computed tomography scan *immediately*.
- D. Send a urinalysis and urine culture.
- E. Perform a pelvic examination.

36.3 A previously healthy 8-year-old boy presents to your clinic with abdominal pain, anorexia, and vomiting that have worsened over the previous 24 hours. The pain is located in the umbilical region. Despite the emesis, he appears well hydrated. A CBC reveals a white blood count of 17,000 cells/mm<sup>3</sup> with 50% polymorphonuclear cells. A urine dipstick on a clean-catch specimen shows 2+ leukocytes and 1+ protein but no nitrites. Which of the following is the most appropriate management at this point?

- A. Obtain a complete chemistry panel and continue to observe him in the office.
- B. Send the patient immediately to the hospital for an abdominal ultrasound.
- C. Give him a prescription for trimethoprim-sulfamethoxazole; schedule a follow-up visit in 2 days to reevaluate the urine.
- D. Admit him to the hospital for intravenous antibiotics to treat presumed pyelonephritis.
- E. Schedule a computed tomography scan of the abdomen for the next morning.

36.4 A 4-year-old girl has a fever of 102.4°F (39.1°C), difficulty swallowing, vomiting, and abdominal pain. Which of the following diagnostic tests is

most likely to yield the appropriate diagnosis?

- A. Streptococcal antigen test (“rapid strep test”)
- B. Antigen test for Epstein-Barr virus (“Monospot”)
- C. Lateral neck radiograph
- D. Abdominal ultrasound
- E. Complete blood count

## ANSWERS

- 36.1 B.** Lower lobe pneumonias can cause abdominal pain, which may be the most distressing symptom in a young patient. Inflammation of the diaphragm can result in an abnormal abdominal examination, which may be mistaken for the source of the child’s illness. This child has cough, fever, tachypnea, and diminished breath sounds, which together make pneumonia the most likely diagnosis.
- 36.2 C.** This adolescent female is at risk for an intra-abdominal abscess despite her appendectomy and intravenous antibiotics. It would be unusual for a urinary tract infection or pelvic inflammatory disease to cause persistent fever despite broad-spectrum intravenous antibiotics.
- 36.3 B.** This boy’s symptoms and signs are most consistent with a diagnosis of acute appendicitis. A urinary tract infection in an otherwise healthy boy would be unusual. His pyuria is most likely the result of bladder wall or ureter irritation caused by an inflamed appendix.
- 36.4 A.** Her symptoms are most consistent with streptococcal pharyngitis. In addition to throat pain and fever, group A *Streptococcus* infections commonly cause abdominal pain and emesis.
- 

## CLINICAL PEARLS

- Acute appendicitis typically causes periumbilical abdominal pain that eventually migrates to the right lower quadrant. Emesis usually follows, rather than precedes, the onset of pain.

- Surgical management of appendicitis occurs as soon as the diagnosis is suspected in order to minimize the potential risks of perforation and intra-abdominal abscess formation.
  - Appendicitis often is not confirmed until surgery. A history and physical examination, urinalysis, CBC, and abdominal ultrasound or computed tomography scan are the most useful tools for eliminating other preoperative considerations.
- 

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### CASE 37

A 19-year-old student presents to the university health center with several days of fever, sore throat, malaise, and a rash that developed today. She first started feeling ill 10 days ago with general malaise, headache, and nausea. Four days ago she developed a temperature of 103°F (39.4°C) that has persisted. She has worsening sore throat and difficulty swallowing solid foods; she is drinking well. She denies emesis, diarrhea, or sick contacts. She takes an oral contraceptive daily and took two doses of ampicillin yesterday (left over from a prior illness). On examination, she is well developed with a diffuse morbilliform rash. She appears tired but in no distress. Her temperature is 102.2° F (39°C). She has mild supraorbital edema; bilaterally enlarged tonsils that are coated with a shaggy gray exudate; a few petechiae on the palate and uvula; bilateral posterior cervical lymphadenopathy; and a spleen that is palpable 3 cm below the costal margin. Laboratory data include



a white blood cell (WBC) count of 17,000 cells/mm<sup>3</sup> with 50% lymphocytes, 15% atypical lymphocytes, and platelet count of 100,000/mm<sup>3</sup>.

- ▶ What is the most likely diagnosis?
- ▶ What is the best study to quickly confirm this diagnosis?
- ▶ What is the best management for this condition?
- ▶ What is the expected course of this condition?

### ANSWERS TO CASE 37: Acute Epstein-Barr Viral Infection (Infectious Mononucleosis)

*Summary:* A female college student has 10 days of malaise, headache, and nausea. She now has a fever, sore throat, and morbilliform rash after taking ampicillin. Her examination reveals a fever, rash, tonsillar hypertrophy with exudate, posterior cervical lymphadenopathy, and splenomegaly. She has an elevated WBC count with a lymphocytic predominance, and a mild thrombocytopenia.

- **Most likely diagnosis:** Epstein-Barr virus (EBV) infection (infectious mononucleosis).
- **Best study:** Assay for heterophil antibodies (Monospot).
- **Best management:** Symptomatic care, avoidance of contact sports while the spleen is enlarged (usually 1-3 months).
- **Expected course:** Acute illness lasts 2 to 4 weeks, with gradual recovery; splenic rupture is a rare but potentially fatal complication. Rarely, some patients have persistent fatigue.

## ANALYSIS

### *Objectives*

1. Describe the presenting signs and symptoms of acute EBV infection.
2. Contrast EBV infection symptoms in young children with those in adolescents and adults.

3. List potential complications of acute EBV infection.

### ***Considerations***

This case is typical for adolescents with primary EBV infection, although supraorbital edema occurs in only 10% to 20% of patients. Differential diagnosis includes group A  $\beta$ -hemolytic streptococcal pharyngitis, but it typically does not have a prodrome similar to this case or cause splenomegaly. Acute cytomegalovirus (CMV) infection is another possibility; similarities include splenomegaly, fever, and atypical lymphocytosis, but exudative sore throat and posterior cervical lymphadenopathy occur less frequently. Although the patient denied recent ill contacts, EBV infection has a 30- to 50-day incubation; further questioning revealed that her boyfriend had similar symptoms 6 weeks ago. Rash is seen less commonly in adolescents with EBV, but many patients develop a morbilliform rash in response to ampicillin, amoxicillin, or penicillin.

APPROACH TO:

### **Epstein-Barr Infection**

## **DEFINITIONS**

**EPSTEIN-BARR VIRUS (EBV):** A double-stranded DNA herpes virus that infects human oropharyngeal and salivary tissues and B lymphocytes. It can cause persistent viral shedding, is associated with oral hairy leukoplakia in HIV-infected adults and lymphoid interstitial pneumonitis in HIV-infected children, and causes several malignancies.

**INFECTIOUS MONONUCLEOSIS:** The typical EBV presentation in older children and adolescents. Fever, posterior cervical adenopathy, and sore throat are seen in more than 80% of cases.

## **CLINICAL APPROACH**

EBV is ubiquitous in humans. In developing nations, infection occurs in almost all children by 6 years of age. In the industrialized world, about half of adolescents have serologic evidence of previous EBV infection; 10% to 15% of previously uninfected college students seroconvert each year. The virus is



excreted in saliva; infection results from mucosal contact with an infected individual or from contact with a contaminated fomite. Shedding of Epstein-Barr virus in the saliva after an acute infection can continue for more than 6 months, and occurs intermittently thereafter for life.

**After an infection occurs, EBV replicates in the oropharyngeal epithelium and later in the B lymphocytes.** A prodromal period may last for 1 to 2 weeks, with vague findings of fever, nausea, malaise, headache, sore throat, and abdominal pain. The sore throat and fever gradually worsen and frequently cause a patient to seek medical help. **Physical findings during an acute infection may include generalized lymph-adenopathy, splenomegaly, and tonsillar enlargement with exudate.** Less common findings include a rash and hepatomegaly.

Primary EBV infection presents as typical infectious mononucleosis in older children and adults, but this presentation is less common in young children and infants. In small children, many infections are asymptomatic. In others, fever may be the only presenting sign. Additional acute findings in small children include otitis media, abdominal pain, and diarrhea. Hepatomegaly and rash are seen more often in small children than in older individuals.

**The Monospot is a useful diagnostic test in children older than approximately 5 years;** the results are unreliable in younger children. Early in the illness the Monospot may be falsely negative. **More definitive testing includes assays of EBV viral capsid antigen (EBV-VCA), early antigen (EA), and Epstein-Barr nuclear antigen (EBNA).** Typically, immunoglobulin (Ig) G and IgM antibodies to EBV-VCA appear first. Anti-EBNA antibodies appear 1 to 2 months following infection and persist for years. Anti-EA antibodies are seen in most children during acute infection and persist for years in approximately one-third of patients. VCA-IgG and EBNA-IgG antibodies indicate past infection. EBV polymerase chain reaction (PCR) is also commercially available, and is distinguished from the above studies by testing for antigen rather than antibody. Other laboratory findings include a **lymphocytic leukocytosis**, with approximately **20% to 40% atypical lymphocytes**. Mild **thrombocytopenia** is common, only rarely precipitating bleeding or purpura. More than half of patients with EBV infection develop **mildly elevated liver function tests**, but jaundice is uncommon.

Infection complications are rare but can be life-threatening. Neurologic sequelae include Bell palsy, seizures, aseptic meningitis or encephalitis, Guillain-Barré syndrome, optic neuritis, and transverse myelitis. Parotitis, orchitis, or pancreatitis may develop. Airway compromise may result from tonsillar hypertrophy; treatment may include steroids. **Splenomegaly** is seen in approximately half of those with infectious mononucleosis; **rupture is rare, but the blood loss is life-threatening.**

Typical infectious mononucleosis requires only rest. Strict bed rest is not useful except for patients with debilitating fatigue. Children with splenomegaly should avoid contact sports to prevent splenic rupture until the enlargement resolves. Acyclovir, which is effective in slowing viral replication, does not affect disease severity or outcome.

Epstein-Barr virus initially was identified from Burkitt lymphoma tumor cells and was the first virus associated with human malignancy. Other associated malignancies include Hodgkin disease, nasopharyngeal carcinoma, and lymphoproliferative disorders. Epstein-Barr virus can stimulate hemophagocytic syndrome. HIV-infected patients may develop oral hairy leukoplakia, smooth muscle tumors, and lymphoid interstitial pneumonitis with EBV infection.

## COMPREHENSION QUESTIONS

- 37.1 A 17-year-old adolescent male has left shoulder and left upper quadrant abdominal tenderness and vomiting. He reports having “mono” last month but says he is completely recovered. He was playing flag football with friends when the pain started an hour ago. On examination, his heart rate is 150 bpm and his blood pressure is 80/50 mm Hg. He is pale, weak, and seems disoriented. He has diffuse rebound abdominal tenderness. Emergent management includes which of the following?
- A. Laparoscopic appendectomy
  - B. Fluid resuscitation and blood transfusion
  - C. Intravenous antibiotics
  - D. Hospital admission for observation
  - E. Synchronized cardioversion for supraventricular tachycardia

37.2 You are in a small town practicing pediatrics and have been asked to see a 2-year-old boy in consultation. His general practice doctor admitted him to the hospital 2 days ago because of 3 days of fever. He has generalized lymph-adenopathy but is otherwise well. Results of Monospot, HIV testing, and CMV antigen tests are negative; his liver function test values are mildly elevated. His physician diagnosed the boy's 7-year-old sibling with "mono" the month prior. You should suggest which of the following?

- A. Start intravenous immunoglobulin and obtain an echocardiogram; the patient likely has Kawasaki disease.
- B. Send an EBV culture for confirmation of the physician's suspicions.
- C. Acyclovir treatment because he has an exposure history positive for EBV.
- D. Obtain EBV-VCA IgG and IgM, EBV-EA, and EBV-NA tests.
- E. Liver imaging with ultrasonography or computed tomography.

37.3 The mother of a 15-year-old adolescent female recently diagnosed with infectious mononucleosis calls for more information. She reports that her daughter, although tired, seems comfortable and is recovering nicely. She remembers that her 20-year-old son had "mono" when he was 10 years old, and he received an oral medicine. She requests the same medication for her daughter. Which of the following is the most appropriate course of action?

- A. Explain that medications are not routinely used in EBV infection.
- B. Call the pharmacy and order oral prednisone 50 mg daily for 5 days (1 mg/kg/d).
- C. Call the pharmacy and order oral acyclovir 250 mg four times per day (20 mg/kg/d).
- D. Have her come to the clinic for a single dose of 50 mg intravenous methylprednisolone (1 mg/kg).
- E. Call the pharmacy and order oral amoxicillin 250 mg three times per day for 7 days.

37.4 A teenage boy arrives for a check-up. His friend recently was diagnosed with mononucleosis. He is worried he will contract it. Which of the

following is true regarding transmission of EBV?

- A. It is common among casual friends.
- B. It occurs only in immunodeficient individuals.
- C. It requires close contact with saliva (ie, kissing or drinking from the same cup).
- D. It is passed only through sexual contact with an infected individual.
- E. It does not occur after the infected person recovers from the initial infection.

## ANSWERS

- 37.1 B.** The patient described is in hypovolemic shock and likely has splenic rupture with intraperitoneal bleeding. He will die shortly if not aggressively resuscitated with fluids and blood. Evaluation by a surgeon for potential removal of the ruptured spleen should follow quickly.
- 37.2 D.** The Monospot heterophil antibody test, useful in older children, is not so reliable in younger children. Antibodies against specific EBV antigens are more helpful in this age group. No imaging study is diagnostic for EBV, and acyclovir is not indicated for EBV exposure. EBV culture is not readily available except in reference laboratories; the antibody studies described above typically are adequate to make the diagnosis. While Kawasaki disease must be considered in patients with persistent fever, the exposure history makes EBV more likely.
- 37.3 A.** Supportive care alone usually is required for a patient with acute EBV infection. Steroids have been used historically; current literature suggests their use only in impending airway compromise due to tonsillar hypertrophy or other life-threatening complications. Acyclovir suppresses viral shedding acutely but has no long-term benefit and is not routinely recommended. Amoxicillin and ampicillin are ineffective antiviral medications and induce a rash in some EBV-infected patients.
- 37.4 C.** EBV is excreted in saliva and is transmitted through mucosal contact with an infected individual (as in kissing) or through a contaminated object. Virus is shed for a prolonged period after symptoms resolve and is intermittently reactivated and shed for years asymptomatically.
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## CLINICAL PEARLS

- Most adults show evidence of past Epstein-Barr virus infection; it is a common infection worldwide.
  - Children in industrialized nations usually are infected with EBV infection later in life than are children in developing countries.
  - Diagnosis of Epstein-Barr virus infection in young children is best achieved by specific antibody assays.
  - Infectious mononucleosis is self-limited and usually does not require treatment. Occasional complications of Epstein-Barr virus infection may require steroid administration.
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## CASE 38

A mother says her 2-year-old daughter has had 1 to 2 weeks of perineal and perianal itching. She notes that the itching occurs mostly at night, but she denies fevers, diarrhea, or emesis. The girl spends time in a “Mother’s Day Out” program 3 days per week but otherwise is always with her mother. On

examination, the perianal area is red and irritated; the anal sphincter tone is normal, and you find no evidence of penetrating trauma. The perineal area is similarly red and excoriated. Other than a slight whitish vaginal discharge, the child's diaper area is clean.

- ▶ What is the most likely diagnosis?
- ▶ How can you confirm the diagnosis?
- ▶ What is the best management for this condition?

#### ANSWERS TO CASE 38: **Pinworms**

*Summary:* A 2-year-old healthy girl with several weeks of nocturnal perianal and perineal pruritus.

- **Most likely diagnosis:** Infection with *Enterobius vermicularis* (pinworms).
- **Confirm the diagnosis:** Cellophane tape test with microscopy to identify pin-worm eggs ([Figure 38-1](#)).



**Figure 38-1.** Pinworm (*Enterobius vermicularis*) ova on microscopy. (Reproduced, with permission, from Rudolph CD, Rudolph AM, Hostetter MK, Lister G, Siegel NJ, eds. *Rudolph's Pediatrics*. 21st ed. New York, NY: McGraw-Hill; 2003:1106.)

- **Best management:** Mebendazole, pyrantel pamoate, or albendazole in a single dose, treating the entire family.

## ANALYSIS

### *Objectives*

1. Describe the presentation of *E vermicularis* infection in the pediatric population.
2. Explain the methods of treatment and prevention of reinfection.

### *Considerations*

This patient has the typical history for pinworm infection. Although sexual abuse is possible, it is unlikely given the history and examination. Poor personal hygiene is another common problem in 2-year-olds who are toilet training and not cleaning themselves adequately. This results in perianal itching and irritation, yet the genital examination will be essentially normal. Occasionally, overzealous cleaning results in similar symptoms.

### APPROACH TO:

#### **Enterobius vermicularis Infection**

## DEFINITION

**NEMATODE (ROUNDWORMS):** Cylindrical organisms, with thousands of different species, only a few of which are parasitic ([Table 38-1](#)). Nematode infection is one of the most common types of infection in humans.



Common Name	Parasite Name(s)	Source of Infection	Signs and Symptoms	Diagnosis	Treatment
Ascariasis	<i>Ascaris lumbricoides</i>	Egg ingestion, usually from soil contaminated with human feces	Most asymptomatic; hemoptysis, pulmonary infiltrates, abdominal pain, distention; occasional intestinal obstruction	Embryonate and non-embryonate eggs in stool; occasionally see adult worms in stool or coughed up	Albendazole single dose, mebendazole for 3 d, or a single dose of pyrantel pamoate; obstruction may be cleared with piperazine salts (causes worm paralysis and expulsion)
Hookworms	<i>Ancylostoma duodenale</i> ; <i>Necator americanus</i>	Larvae in soil penetrate exposed skin	Pruritus and rash at site of entry; epigastric pain and diarrhea; anemia from blood loss; respiratory symptoms	Characteristic ovoid eggs in stool	Mebendazole for 3 d, or albendazole single dose, or pyrantel pamoate; may include iron supplement; a hookworm vaccine is in development



Pinworms	<i>Enterobius vermicularis</i>	Egg ingestion	Many asymptomatic; nocturnal perianal itching most common	Microscopy of cellophane tape applied to anus reveals eggs; routine stool ova and parasites not useful	Pyrantel pamoate, or mebendazole, or albendazole single dose with a second dose 2-3 wk later
Strongyloids	<i>Strongyloides stercoralis</i>	Larvae penetrate skin and move to lungs and then intestines; also auto-infectious, larvae can move from intestines into blood stream, to lungs, and back to intestines	Can be asymptomatic; can cause epigastric pain, emesis, diarrhea, malabsorption, weight loss	Larvae in feces, or sample of duodenal fluid by a string test	Ivermectin for 1-2 d, or thiabendazole for 2 d; may require up to 2 wk of therapy, based on subsequent stool examinations

Visceral and ocular larva migrans	<i>Toxocara canis</i> ; <i>Toxocara cati</i> ; <i>Toxocara leonina</i> ; <i>Baylisascaris procyonis</i>	Egg ingestion, usually from soil contaminated with dog or cat feces	Fever, cough, occasional abdominal pain; hepatomegaly, rhonchi, and skin lesions on examination	Clinical presentation and serologic testing; significant eosinophilia (>20%) with leukocytosis; microscopy of affected tissue occasionally reveals larvae	Visceral: none, self-limited disease Ocular: diethylcarbamazine, albendazole for 3-5 d, or mebendazole for 5 d; use with caution, as death of organisms may precipitate inflammatory reaction
Whipworms	<i>Trichuris trichiura</i>	Egg ingestion	Most asymptomatic; can cause proctitis, bloody diarrhea, abdominal pain, rectal prolapse	Lemon-shaped eggs in the stool	Mebendazole or albendazole for 3 d (single dose for light infections)

**Table 38-1 • COMMON NEMATODE INFECTIONS IN HUMANS**

## CLINICAL APPROACH

A patient with perianal itching, especially at night, should be evaluated for *E. vermicularis* infection. Unlike many other parasites, feces examination for ova is not useful because the eggs are small and few. Some parents may see a worm in the stool, but *E. vermicularis* is difficult to identify positively with the naked eye. Instead, **cellophane tape is applied to the perianal region in the early morning**; from this tape *E. vermicularis* eggs may be identified with microscopy. These eggs are infectious; proper infection control practices are indicated.

***Enterobius vermicularis* infection** is the **most common nematode infection in North America**, and humans are the only natural host. Risk factors include exposure to other children in a day care environment or in the home. The adult worm is approximately 1 cm long and lives in the human GI tract, rarely migrating to the appendix, spleen, liver, bladder, and vagina. The pinworm life cycle begins when female worms migrate to the perianal region to deposit their eggs. Within 6 hours a larva is present in each ovum; the larvae are viable for up to 20 days. These eggs are subsequently transferred to clothes, fingers (from itching), and bed sheets. An infection results upon egg ingestion. The larvae “hatch” in the duodenum and grow to adult worms in 4 to 6 weeks.

Many infected patients are asymptomatic. The symptom described most frequently is **nocturnal perianal itching**, a result of worm and ova hypersensitivity. The gravid worms occasionally migrate to the perineal area, resulting in vaginal itching and discharge. Although bruxism historically has been related to pinworm infection, perianal itching is the only consistently reported symptom.

Some experts recommend treating the entire family (but at least washing all potentially infected bedding); others suggest global treatment only in recurrent cases. **Treatment can be with mebendazole, albendazole, or pyrantel pamoate** in a single dose. Often a second dose is given 2 weeks after the first dose to eliminate any new worms released from ova ingested proximate to the treatment time.

## COMPREHENSION QUESTIONS

- 38.1 A mother states that her 4-year-old son has had 2 days of “buttocks pain.” She reports several blood-streaked stools and frequent scratching of the area. He is afebrile, but his perianal region is bright red with a clearly demarcated erythematous border. The area is diffusely tender, but no nodularity, fluctuance, or trauma is found. Appropriate diagnostic testing and therapy include which of the following?
- A. Stool sample for ova and parasites; treatment with albendazole
  - B. Cellophane tape test for ova; treatment with albendazole
  - C. Rapid streptococcal test of the anal area; oral antibiotics

- D. Blood culture; parenteral antibiotics
- E. Administration of diaper rash ointment

38.2 A 6-year-old boy who recently moved from the southeastern United States complains of “something coming out” of his buttocks while straining during defecation; it seems to resolve when he relaxes. He also complains of abdominal pain and bloody stools for the last week. Examination reveals a normal external anus without evidence of trauma. When straining, he produces a pink mucosal mass from his anus; it returns when he relaxes. Initial diagnostic evaluation should include which of the following studies?

- A. Cellophane tape test upon morning awakening
- B. Stool for ova and parasites
- C. Rectal culture
- D. Abdominal ultrasonography
- E. Herpes culture

38.3 A mother brings a stool sample for your review. In the stool are several 15- to 20-cm long, round, whitish worms. You initiate treatment with which of the following?

- A. Amoxicillin
- B. Mebendazole
- C. Praziquantel
- D. Niclosamide
- E. Paromomycin

38.4 A 14-year-old adolescent male with HIV and AIDS presents for a physical examination prior to traveling to Southeast Asia. In counseling him on health risks in the area, you mention that he must always wear shoes to help prevent *Strongyloides* infection, which is particularly dangerous to him for which of the following reasons?

- A. His antiretroviral medications make him more susceptible.
- B. His immunodeficiency will make eradication impossible.
- C. Antiparasitic agents are not available in Southeast Asia.

D. Teenagers typically have severe disease when infected.

E. *Strongyloides* can develop a “hyperinfection” in immunocompromised hosts.

## ANSWERS

- 38.1 C. Although diagnostic considerations should include pinworm infestation (as well as sexual abuse, contact diaper rash, and candidal diaper rash), the presentation is more consistent with perianal cellulitis. Pinworm infection usually does not cause blood-streaked stool, and any erythema associated with it is not well demarcated. Perianal cellulitis is commonly caused by *Streptococcus* and usually responds to oral or topical (mupirocin [Bactroban]) antibiotics.
- 38.2 B. Pinworms are not known to cause rectal prolapse, but whipworms (*Trichuris trichiura*) are. The whipworm nematode lives in warm and humid areas and is commonly found in the rural southeastern United States. Routine microscopy for ova is sufficient for the diagnosis (whipworms produce many more ova than do pinworms). Treatment is albendazole or mebendazole. Cystic fibrosis should be a consideration in a child with rectal prolapse, although the history should also include frequent pneumonias, failure to thrive, or foul-smelling stools.
- 38.3 B. Worms of this size and description typically are *Ascaris*; treatment is mebendazole or albendazole. Amoxicillin is an antibacterial agent. Praziquantel, niclosamide, and paromomycin are effective against cestodes (tapeworms) and are not recommended for nematodes.
- 38.4 E. The life cycle of *Strongyloides* does not require a period outside the host. Therefore, the organism can “autoinfect” the host (larvae in the intestines move through the intestinal wall, into the circulation, through the lungs, and back into the intestines). This autoinfection can lead to disseminated strongyloidiasis in immunocompromised hosts with massive invasion of organs and subsequent tissue destruction; sepsis with gram-negative intestinal organisms can result.

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## CLINICAL PEARLS

- Patients with nocturnal perianal itching are evaluated for *Enterobius vermicularis* infection.
  - Typical stool ova and parasites studies may not identify *Enterobius vermicularis* ova (the count is low). A cellophane tape test is more useful to confirm the diagnosis.
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### CASE 39

A 5-month-old infant arrives at the emergency center strapped to a backboard with a cervical collar in place. The father was holding him in his lap in the front passenger seat of their sedan when the driver lost control and crashed. The child was ejected from the car through the windshield. The paramedics report that his modified Glasgow coma scale score is 6 (opens eyes to painful stimuli, moans to painful stimuli, and demonstrates abnormal extension); they intubated him at the scene. He had a self-limited, 2-minute generalized tonic-clonic seizure en route to the hospital.

Your assessment reveals a child with altered mental status. His endotracheal tube is in the correct position, and his arterial blood gas reflects effective oxygenation and ventilation. He is euthermic and tachycardic. He has no evidence of fractures, and his abdominal examination is benign. He has

several facial and scalp lacerations. His anterior fontanelle is bulging, his sutures are slightly separated, and his funduscopy examination reveals bilateral retinal hemorrhages.

- ▶ What is the most likely etiology for this child's altered mental status?
- ▶ What is the most appropriate study to confirm this etiology?

### ANSWERS TO CASE 39: **Subdural Hematoma**

*Summary:* An unrestrained infant is ejected through the windshield. He has altered mental status, he has experienced seizure activity, and his examination is consistent with increased intracranial pressure (ICP).

- **Most likely diagnosis:** Subdural hematoma.
- **Best study:** Emergent computed tomography (CT) of the head.

## ANALYSIS

### *Objectives*

1. Describe the typical clinical findings in head trauma.
2. Compare the typical findings of subdural hematoma with those of epidural hematoma.
3. Discuss the possible treatment options for intracranial hemorrhage.

### *Considerations*

This child is younger than 1 year, and subdural hematomas are more common in this age group; epidural hematomas are more common in older children. Seizures are more common with subdural hematomas, occurring in 75% of affected patients; seizures occur in less than 25% of epidural hematoma patients. His altered mental status could be caused by a simple cerebral concussion, but the CT scan would be normal or show nonspecific changes. The infant's ejection at the crash provides an appropriate mechanism of injury, making other considerations (such as shaken baby syndrome, more recently referred to as abusive head trauma) less likely. This child's lack of a car seat must also be addressed.



APPROACH TO:

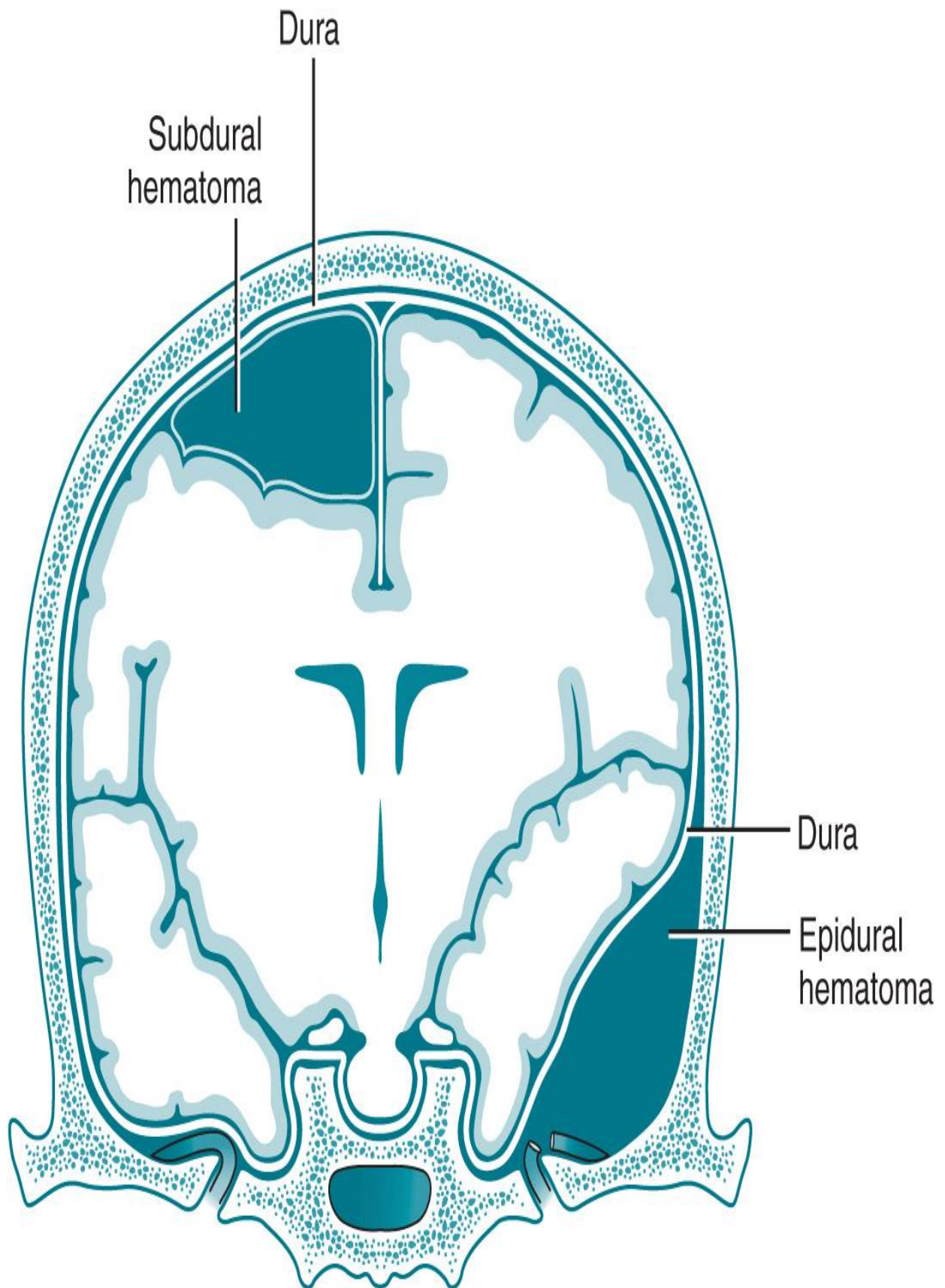
**Subdural Hematoma**

## **DEFINITIONS**

**CONCUSSION:** Altered mental state immediately after blunt head trauma; no consistent brain abnormality is seen; can cause retrograde and anterograde memory loss.

**EPIDURAL HEMORRHAGE:** Bleeding between the dura and the skull; commonly occurs with skull fracture and middle meningeal artery laceration but can result from disruption of dural sinuses or middle meningeal veins ([Figure 39-1](#)).





**Figure 39-1.** Anatomy of subdural and epidural hematomas.

**GLASGOW COMA SCALE (GCS):** A clinical tool developed to assist in head injury severity prediction. For infants and toddlers, several “modified” scales exist that attempt to adapt the verbal portion to reflect language development and modify the motor component to reflect the lack of purposeful movement in early infancy ([Table 39-1](#)).

Eye opening:	
1	None
2	To pain
3	To speech
4	Spontaneous
Verbal communication:	
1	No response
2	Incomprehensible sounds
3	Inappropriate words
4	Confused conversation, cries
5	Oriented, cries to indicate needs
Motor response:	
1	None
2	Abnormal extension
3	Abnormal flexion
4	Withdraws from pain
5	Localizes pain
6	Spontaneous movement in infants <6 mo and goal-directed movements in children 6 to 36 mo

## **Table 39-1 • MODIFIED GLASGOW COMA SCORE FOR CHILDREN YOUNGER THAN 3 YEARS OF AGE**

**SUBDURAL HEMORRHAGE:** Bleeding between the dura and the arachnoid space; occurs with disruption of bridging veins connecting cerebral cortex and dural sinuses ([Figure 39-1](#)).

## **CLINICAL APPROACH**

The child in the case is seriously ill, with evidence of increased ICP and retinal hemorrhages. Some form of cerebral hemorrhage is likely. Initial management follows the **ABCs** of resuscitation: evaluate the patient's **A**irway first, followed by his **B**reathing, and then his **C**irculatory status. Care can then be directed at his injuries.

**Subdural hemorrhage is more common in children younger than 1 year and is far more common than a supratentorial epidural hemorrhage. Approximately one-third of CT-identified subdural hemorrhages have an associated skull fracture;** almost all are venous in origin, and approximately **three-fourths are bilateral.** The CT images typically show a crescentic hematoma. **Seizures occur in 60% to 90% of afflicted patients,** and retinal hemorrhages are frequently associated. Increased ICP is typical. Subdural hemorrhage is generally associated with less mortality than that seen with epidural hemorrhage, but long-term morbidity is more significant because the brain parenchyma is more often involved.

Subdural hematomas may be acute, subacute, or chronic. In acute hematomas, symptoms occur in the first 48 hours after injury. Patients with subacute subdural hematoma display symptoms between 3 and 21 days after injury, whereas chronic hematomas cause symptoms after 21 days. **Chronic subdural hematomas are more common in older children** than in infants; symptoms may include chronic emesis, seizures, hypertonicity, irritability, personality changes, inattention, poor weight gain, fever, and anemia. Magnetic resonance imaging is more useful than CT for evaluating subacute and chronic hematomas because the hematoma age can be estimated by signal intensity.

**Epidural hemorrhages occur more commonly in older children and adults** and are seen more typically in the infratentorial space. **Two-thirds of**

**epidural hemorrhages are associated with skull fracture.** Although most adult epidural hemorrhages are arterial in origin, in children approximately half originate from venous injuries. **Most epidural hemorrhages are unilateral,** are located in the temporoparietal region, and present on CT scan as a lens-like, or biconvex, hematoma. **Fewer than 25% of epidural hematoma patients have seizures,** and retinal hemorrhages are uncommon. **Mortality is greater with epidural hemorrhage than with subdural hemorrhage,** but in survivors long-term morbidity is low.

Increased ICP, which can be caused by both hemorrhage forms, is important to recognize and treat. Epidural hematomas are frequently rapidly progressive and may require urgent surgical evacuation with identification of the bleeding source. Subdural hemorrhage usually does not require urgent evacuation but may require evacuation at a later date.

## COMPREHENSION QUESTIONS

- 39.1 You are the team physician for a local high-school football team. During the first quarter of a district playoff game, you watch as your star quarterback is sacked with a helmet-to-helmet tackle. He does not get up from the initial impact. You sprint onto the field with the trainer and assess the injured player. He is breathing and has a steady pulse, but he is unconscious. As you continue your evaluation, he wakes up. He remembers his name but cannot remember the day, his position in the team, or how he got to the game. He has no sensory or motor deficit suggestive of a cervical spine injury, and you assist him off the field. After 15 minutes he is fully oriented and wants to go back in. The coach tells him he is sitting out for the rest of the game. The player appeals to you. Which of the following is the most appropriate management?
- A. Affirm the coach's decision. Tell the player that he will need sequential evaluations before he can come back to practice.
  - B. Affirm the coach's decision. Tell the player he can come back and attend regular practice tomorrow.
  - C. Refute the coach's decision. Tell the player he can resume playing now.

D. Refute the coach's decision. Tell the player he can resume playing after half-time.

E. Strap the player to a backboard and take him to the hospital.

**39.2** A 17-year-old adolescent female is brought to the hospital after a motor vehicle crash. She and her boyfriend had been drinking beer and were on their way home when she lost control of the car and hit the side wall of the local police station. She reportedly had a brief loss of consciousness but currently is oriented to name, place, and time. She responds appropriately to your questions. While waiting for her cervical spine series, she vomits and lapses into unconsciousness. She becomes bradycardic and develops irregular respirations. Which of the following brain injuries is most likely in this case?

A. Subdural hemorrhage

B. Epidural hemorrhage

C. Intraventricular hemorrhage

D. Posttraumatic epilepsy

E. Concussion

**39.3** Several days after emergent management, the adolescent in Question 39.2 is transferred to your general inpatient ward service from the intensive care unit. She is concerned about her prognosis. Which of the following statements is correct?

A. She will need extensive neuropsychiatric evaluation before she can return to school.

B. She will likely have headaches, fatigue, nausea, and sleep disturbances.

C. She will likely develop seizures and needs 2 years of prophylactic seizure medicine.

D. She can no longer be legally permitted to drive because she has had brain surgery.

E. She should have few long-term problems.

**39.4** A 7-month-old child presents to the emergency room after reportedly falling from his high chair. The parents report no loss of consciousness, other trauma, or medical problems. Your examination reveals a few old

bruises but no evidence of acute trauma or fracture. He is irritable, so you request a CT scan of the brain without contrast. The pediatric radiologist reports bilateral frontal subdural hematomas and notes two healing skull fractures that she estimates to be approximately 2 weeks old. Which of the following is the best next step in this child's management?

- A. Observe him for 6 hours in the emergency center.
- B. Assess bleeding time and prothrombin time.
- C. Order magnetic resonance imaging of the head.
- D. Discharge him from the emergency center with head injury precautions.
- E. Order an electroencephalography and a neurology consultation.

## ANSWERS

- 39.1 A.** Although controversial, the correct answer is for a player who sustains a concussion resulting in loss of consciousness to refrain from play for the remainder of the day. The most recent clinical report from the American Academy of Pediatrics concerning conditions affecting sports participation references the 3rd International Conference on Concussion in Sports from 2008. This report suggests that individualized and frequent reassessment over time, and a stepwise return to play, is more useful than a predetermined length of time to refrain from additional sports.
- 39.2 B.** This teen displays the typical adult course of epidural hemorrhage (an initial period of altered mental status [initial concussion], a period of lucidity, and then redevelopment of altered mental status and symptoms of increased ICP [hematoma effect]). Younger children typically do not display this pattern. Immediate neurosurgical evaluation is required.
- 39.3 E.** The acute epidural hemorrhage mortality rate is higher than that of acute subdural hemorrhage, but long-term morbidity in survivors is less. The complaints in answer B are common after a subdural hemorrhage. A seizure disorder may preclude driving; a cranial surgery history does not.
- 39.4 C.** This child has evidence of old skull fractures with subdural hematomas. Head magnetic resonance imaging would help to determine



the hematoma age. If the hematoma blood age correlates with the estimated skull fracture age, child abuse is considered. Neurology may be helpful later, but an immediate consultation would be of limited benefit before additional data were gathered. Discharge with the information presented in the case is dangerous; the child likely requires hospital admission and the involvement of social services. Bleeding studies are unlikely to be helpful initially but may be required at some point if child abuse is suspected and a court case is anticipated. The child has no history consistent with a bleeding disorder, and a bleeding disorder does not explain the old fractures.

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### CLINICAL PEARLS

- Subdural hemorrhage is more common in children younger than 1 year and in the supratentorial space; seizures and retinal hemorrhages are frequently associated findings, and increased ICP is typical.
  - Epidural hemorrhages are more commonly seen in older children and adults and in the infratentorial space. Fewer than 25% of patients have seizures; retinal hemorrhages are uncommon.
  - Mortality with subdural hemorrhage is generally less than that seen with epidural hemorrhage, but long-term morbidity is more significant with subdural injury because the brain parenchyma is more often involved.
- 

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#### CASE 40

A 16-year-old adolescent female presents to your clinic complaining of very heavy menstrual bleeding for the last 6 months. She notes that her cycles are regular, occurring every 29 days, but they last for 10 days and she goes through 10 to 12 pads per day. Her last period ended a week ago, and she now complains of dizziness when she stands up. She denies concurrent vaginal discharge or abdominal pain. Her past medical and family histories are negative for bleeding problems. Her menarche was at 12 years of age, and she started having regular menstrual cycles at 14 years of age. She denies all forms of sexual activity. Her examination is significant for mild resting tachycardia and orthostatic hypotension. Her nail beds and conjunctiva are pale. A urine pregnancy test is negative, and her hemoglobin is 10 g/dL.

- What is the most likely diagnosis?
- How would you manage this patient?

#### ANSWERS TO CASE 40: **Dysfunctional Uterine Bleeding**

*Summary:* An adolescent female complains of heavy but regular menstrual bleeding that has resulted in anemia and orthostatic hypotension.

- **Most likely diagnosis:** Dysfunctional uterine bleeding (DUB).
- **Management:** Iron supplement and monophasic low-dose oral contraceptive pills (OCPs) for 3 to 6 months with a follow-up hemoglobin in 6 weeks.

## ANALYSIS

### *Objectives*

1. List the diagnostic possibilities for abnormal uterine bleeding.
2. Describe the appropriate evaluation of abnormal uterine bleeding.
3. Differentiate between the different managements of DUB based on symptoms and type of bleeding.

### *Considerations*

Menstrual bleeding that leads to anemia and orthostatic hypotension is not typical, and requires further investigation. Excessive bleeding may be caused by pregnancy; although she denies sexual activity, a urine pregnancy test should be part of the evaluation. Sexually transmitted diseases, malignancy, and trauma should also be considered.

### APPROACH TO:

#### **Dysfunctional Uterine Bleeding**

## DEFINITIONS

**MENORRHAGIA:** Excessive and/or prolonged uterine bleeding with a regular menstrual cycle.

**METRORRHAGIA:** Irregular uterine bleeding between menstrual cycles.

**MENOMETRORRHAGIA:** Irregular uterine bleeding with excessive and/or prolonged flow.

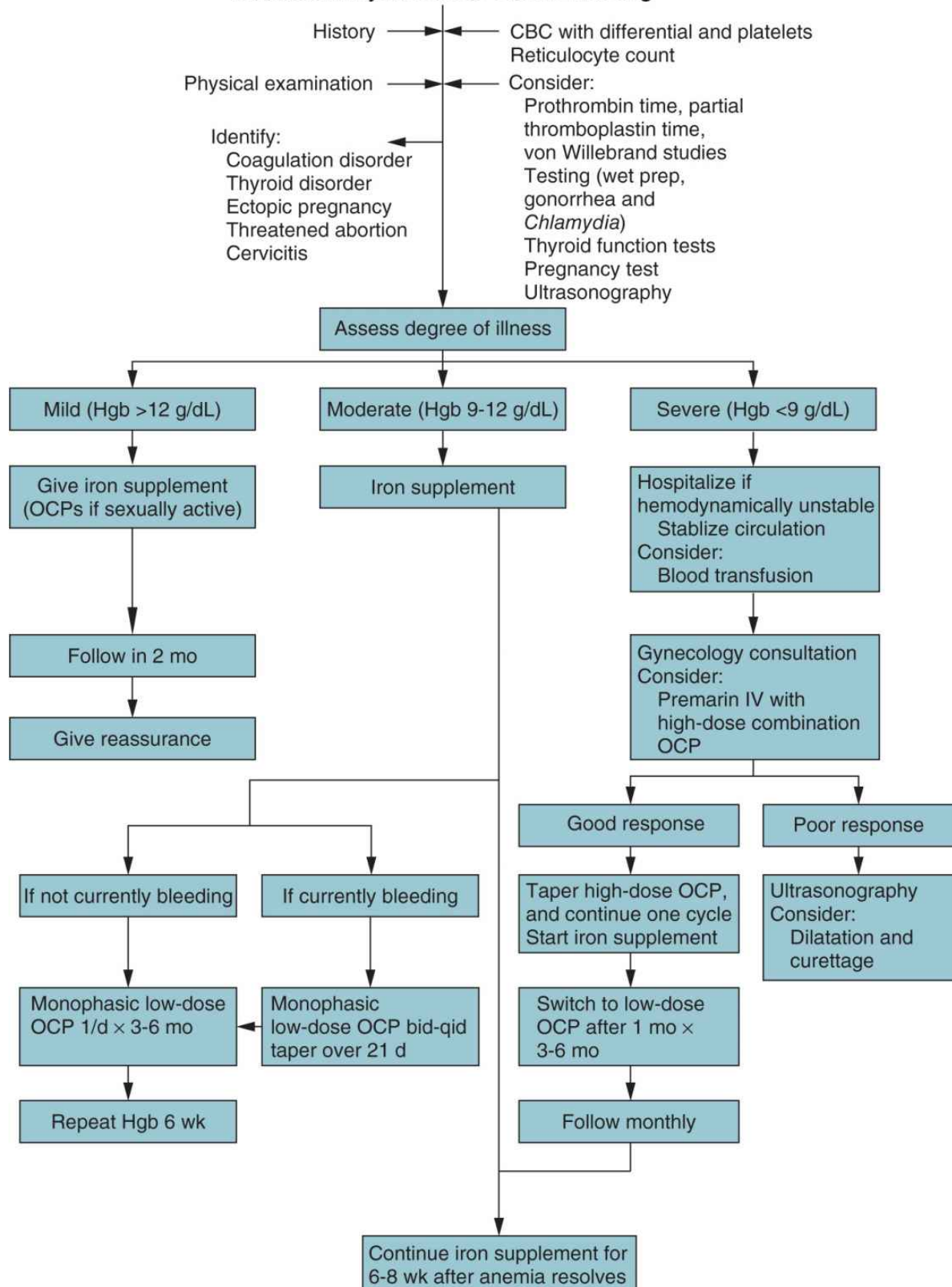
## CLINICAL APPROACH

Dysfunctional uterine bleeding is abnormal flow that occurs either excessively in a regular cycle (menorrhagia) or irregularly and not related to the normal menstrual flow (metrorrhagia). Dysfunctional uterine bleeding is a diagnosis of exclusion; other diagnoses must be considered first. Of young women presenting with abnormal vaginal bleeding, about 9% will have an organic cause such as ectopic pregnancy or threatened abortion; other potential causes include infections (cervicitis, human papillomavirus [HPV], trichomonas), trauma, hormonal contraceptives and other medications, hypothyroidism, foreign body, or malignancy. The remainder of women will have no demonstrable cause for their bleeding and are diagnosed with dysfunctional, or abnormal, uterine bleeding.

The typical presentation is that of a teen with regular menstrual cycles who then develops prolonged or heavy menstrual bleeding, or irregular bleeding. The bleeding is usually painless. Important aspects of the history include prior episodes of bleeding, the length of the woman's cycle, the number of days of bleeding, and the severity of the bleeding (can be established by asking about the number of pads or tampons used per day). Family history should include others with bleeding problems such as excessive hemorrhage after surgery and women requiring hysterectomy after childbirth.

After verifying the patient is not pregnant, the next most important laboratory evaluation is the hemoglobin. The degree of anemia helps categorize the severity of bleeding and helps guide management ([Figure 40-1](#)). Women with a hemoglobin more than 12 g/dL are considered to have mild bleeding, and may be managed with iron supplements alone and with careful follow-up. A hemoglobin of 9 to 12 g/dL is considered a result of moderately severe bleeding; treatment includes iron and monophasic OCP. Women with a hemoglobin less than 9 g/dL are considered to have severe bleeding, and may need hospitalization and transfusion. Intravenous estrogen (Premarin) and high-dose oral contraceptives are used until the bleeding stops; further bleeding despite these measures may require dilatation and curettage. Although these high doses of estrogen raise theoretical concerns about thrombotic events, none have been reported with the short-term use required in this condition.

## Patient with Dysfunctional Uterine Bleeding



**Figure 40-1.** Evaluation of dysfunctional uterine bleeding. CBC, complete blood count; Hgb, hemoglobin; OCP, oral contraceptive pills. (Reproduced, with permission, from Kaplan DW, Love-Osborne L. Adolescence. In: Hay WW, Levin MJ, Sondheimer JM, Deterding RR, eds. *Current Diagnosis and Treatment in Pediatrics*. 19th ed. New York, NY: McGraw-Hill; 2009:128.)

Patients with dysfunctional uterine bleeding continue oral contraceptives for 3 to 6 months. After the menstrual cycle is regular and irregular bleeding has ceased, careful withdrawal of the OCP may be attempted if desired with close follow-up. Iron supplementation should be continued for 2 months after the anemia is resolved.

## COMPREHENSION QUESTIONS

- 40.1 A 15-year-old adolescent female presents to the local hospital emergency center complaining of several days of left-sided abdominal pain, mild vaginal bleeding, and dizziness. Upon further questioning you learn that she has had near-syncopal episodes the last few times she has tried to stand up. She denies fever, sexual activity, previous episodes of mid-cycle vaginal bleeding, and abdominal or genitourinary trauma. On examination, she is pale and tachycardic. She has abdominal pain with rebound and guarding in the upper and lower left quadrants that radiates to the back. Her hemoglobin is 5 g/dL, her white count is 12,000/mm<sup>3</sup>, and her platelet count is 210,000/mm<sup>3</sup>. Her serum B-HCG is 1800 mIU/mL. Which of the following is the most likely diagnosis?
- A. Metrorrhagia with subsequent anemia
  - B. Pelvic inflammatory disease
  - C. Salicylate overdose
  - D. Ruptured ectopic pregnancy
  - E. Uterine malignancy
- 40.2 A 13-year-old adolescent female comes to the office for a preparticipation sports physical before the start of the basketball season. She has no complaints, but wants to discuss the human papillomavirus (HPV) vaccine some of her friends have received. Which of the following is an accurate statement about human papillomavirus and the vaccine?

- A. The HPV vaccine is indicated only once a woman becomes sexually active.
- B. HPV types 6 and 11 are high cancer risk serotypes and are included in the vaccine.
- C. HPV vaccine helps prevent cervical cancer but not genital warts.
- D. HPV types 16 and 18 are associated with the majority of cervical cancers.
- E. Syncope after injection has been reported and is a unique adverse reaction to HPV vaccine.

40.3 A 16-year-old presents to your clinic with a complaint of persistent vaginal bleeding. She had been seen 3 months ago when you noted a mild anemia of 13 g/dL, diagnosed her with dysfunctional uterine bleeding, and started her on iron supplements. Today she is listless and pale. Her hemoglobin in your clinic is 6 g/dL, her platelet count is normal, and her urine pregnancy test remains negative. You admit her to your local hospital and order a transfusion of packed red blood cells. In addition to stabilizing her circulatory system, which of the following is the most appropriate next step in the acute management of her condition?

- A. Monophasic low-dose oral contraceptive (OCP)
- B. Intravenous conjugated estrogens (Premarin) and high-dose combination OCP
- C. Hysterectomy
- D. Discharge after transfusion with iron supplementation
- E. Triphasic low-dose OCP

40.4 A 19-year-old adolescent female presents with a temperature of 101.2°F (38.4°C), lower abdominal pain, bloody vaginal discharge, and dyspareunia. She has no nausea or vomiting, and is tolerating fluids well. She has cervical motion tenderness on examination. Her urine pregnancy test is negative, and an ultrasound of her right lower quadrant is negative for appendicitis. Which of the following is the appropriate outpatient management for her likely condition?

- A. Levofloxacin, 500 mg orally once a day for 14 days as monotherapy
- B. Ofloxacin, 400 mg orally twice a day for 14 days as monotherapy

- C. Ceftriaxone, 250 mg IM in a single dose as monotherapy
- D. Levofloxacin, 500 mg orally once a day, and doxycycline, 100 mg orally twice a day, both for 14 days
- E. Ceftriaxone, 250 mg IM as a single dose and doxycycline, 100 mg orally twice a day for 14 days

## ANSWERS

- 40.1 D.** The classic triad of abdominal pain, vaginal bleeding, and amenorrhea only occurs in about 50% of cases of ectopic pregnancy. As ectopic pregnancy is the leading cause of pregnancy-related death in the first trimester; a physician must consider the diagnosis for any woman of childbearing age with abdominal pain. Risk factors for an ectopic pregnancy include pelvic inflammatory disease (PID), intrauterine device (IUD), previous ectopic pregnancy, previous tubal surgery, increasing age, use of fertility drugs, and smoking. Since this patient is hemodynamically unstable, admission and surgery are indicated; however, hemodynamically stable patients with an unruptured ectopic pregnancy and good follow-up may be managed expectantly or treated with methotrexate.
- 40.2 D.** Quadrivalent human papillomavirus vaccine (Gardasil) was licensed in 2006, and is indicated for the prevention of HPV types 6, 11, 16, and 18. Types 6 and 11 cause about 90% of all genital warts, but carry a low risk of malignancy. Types 16 and 18 cause about two-thirds of all cervical cancer cases. Immunization before sexual debut is ideal, but even women who are sexually active may benefit from the vaccine; as there is no commercially available screening test to determine the serotypes to which a woman has been exposed, the vaccine may still provide some protection. Boys, too, receive this vaccination beginning at the age of 11 years in the effort to prevent warts and spread of the virus. The vaccine is a three-dose series. Common side effects include headache and pain at the injection site. Anaphylaxis to yeast is a contraindication. Syncope has been reported in the adolescent population with all vaccines; current recommendations suggest observing adolescents for 15 minutes after immunization.



- 40.3 **B.** Based on her anemia, this adolescent's dysfunctional uterine bleeding is classified as severe, and warrants hospitalization. Stabilization of her circulatory system is the first priority, and then steps must be taken to stop the bleeding. Intravenous conjugated estrogens (Premarin) in conjunction with a high-dose OCP is the next step. If this treatment is successful in decreasing the bleeding, she can be continued on high-dose OCP for a month and then moved to a low-dose OCP. If she continued to have bleeding after IV Premarin and a high-dose OCP, dilatation and curettage may be necessary.
- 40.4 **E.** More than one million women develop pelvic inflammatory disease (PID) in the United States each year, and more than a quarter of these require hospitalization. PID is most common in the teen population, with decreasing incidence with increasing age. As presenting signs and symptoms are variable, diagnosis can be difficult. The Centers for Disease Control and Prevention (CDC) recommends that empiric treatment should be started if a young woman at risk for PID presents with lower abdominal or pelvic pain, no other cause for the pain can be identified, and the woman has: (1) cervical motion tenderness, (2) uterine tenderness, or (3) adnexal tenderness. Treatment is aimed at both gonorrhea and chlamydia. Recent surveillance by the CDC has shown fluoroquinolone-resistant gonorrhea is widespread in the United States, so fluoroquinolones are no longer recommended in the treatment of PID.
- 

### CLINICAL PEARLS

- Pregnancy and STDs must be considered in any adolescent with abnormal vaginal bleeding.
  - Dysfunctional uterine bleeding can be excessive flow with normal intervals (menorrhagia), or flow with irregular intervals (metrorrhagia).
  - Cessation of bleeding can usually be achieved through the use of oral contraceptives; occasionally, intravenous estrogen is required.
- 

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## CASE 41

The emergency department (ED) notifies you that one of your patients is being evaluated for new-onset seizures. The 2-year-old boy was in his normal state of good health until this morning, when he complained of a headache and then fell to the floor. While waiting for the ED physician to come to the phone, you review the patient's chart and find that he has had normal development. His family history is significant for a single seizure of unknown etiology in his father at 4 years of age. According to the ED physician, the boy's mother saw jerking of both arms and legs. When the ambulance arrived 5 minutes later, the child had stopped jerking but was not arousable; his heart rate was 108 bpm, respiratory rate 16 breaths/min, blood pressure 90/60 mm Hg, and

temperature 104°F (40°C). His blood sugar level was 135 mg/dL. By the time the child arrived to the ED, he was awake and he recognized his parents. His physical examination in the ED is significant only for a red bulging immobile tympanic membrane. His complete blood count and urinalysis are normal.

- ▶ What is the most likely diagnosis?
- ▶ What is the best management for this condition?
- ▶ What is the expected course of this condition?

### ANSWERS TO CASE 41: **Simple Febrile Seizure**

*Summary:* An otherwise normal 2-year-old boy, with a family history of a single seizure in his father at 4 years of age, has a brief, generalized, self-limited seizure associated with an elevated temperature. His examination is nonfocal. He has completely recovered within 1 to 2 hours of the seizure.

- **Most likely diagnosis:** Simple febrile seizure.
- **Best management:** Parental education, injury prevention during seizures, and fever control.
- **Expected course:** More seizures with fever may occur, but he is likely to “grow out” the condition by 5 to 6 years of age. He is likely to have no sequelae and is expected to have normal development.

## ANALYSIS

### *Objectives*

1. Describe a typical febrile seizure.
2. Explain the typical course of febrile seizures.
3. List factors that increase the risk of further seizure activity.

### *Considerations*

This patient likely had a simple febrile seizure. The seizure was short, self-limited, and generalized without focal findings. The child had an elevated temperature and is between the ages of 6 months and 6 years. He had a short

postictal state and then quickly returned to normal. He is old enough to have reliable neck examination findings and has no evidence of meningeal irritation. The father might have had a febrile seizure; data are insufficient to make that conclusion.

APPROACH TO:

**Febrile Seizure**

## DEFINITIONS

**EPILEPSY:** Recurrent seizure activity; may or may not have identifiable cause.

**FEBRILE SEIZURE:** A seizure occurring in the absence of central nervous system (CNS) infection with an elevated temperature in a child between the ages of 6 months and 6 years.

**SEIZURE:** Abnormal electrical activity of the brain resulting in altered mental status and/or involuntary neuromuscular activity.

## CLINICAL APPROACH

A diagnosis of febrile seizure must be made only after considering CNS infection as the cause. **Two classic physical findings** suggest **meningeal irritation**: **Kernig sign** (patient is supine, leg flexed at the hip and knee at 90° angle, pain is induced with leg extension) and **Brudzinski sign** (while supine, passive neck flexion results in involuntary knee and hip flexion). If the **neurologic examination is abnormal** after the seizure, the **seizure occurred several days into the illness**, or if the **child is unable to provide adequate feedback** during a neck examination, a **lumbar puncture (LP)** may be **necessary**. The meningeal signs described above usually are **not reliable in children younger than 1 year**; therefore, an **LP is recommended for such patients with fever and seizure**. **Contrast-enhanced brain imaging** should occur before LP when a **space-occupying lesion**, such as a brain abscess, is a possibility.

**Febrile seizures** are a uniquely pediatric entity. **Typically occurring between 6 months and 6 years of age**, these convulsions are distressing to

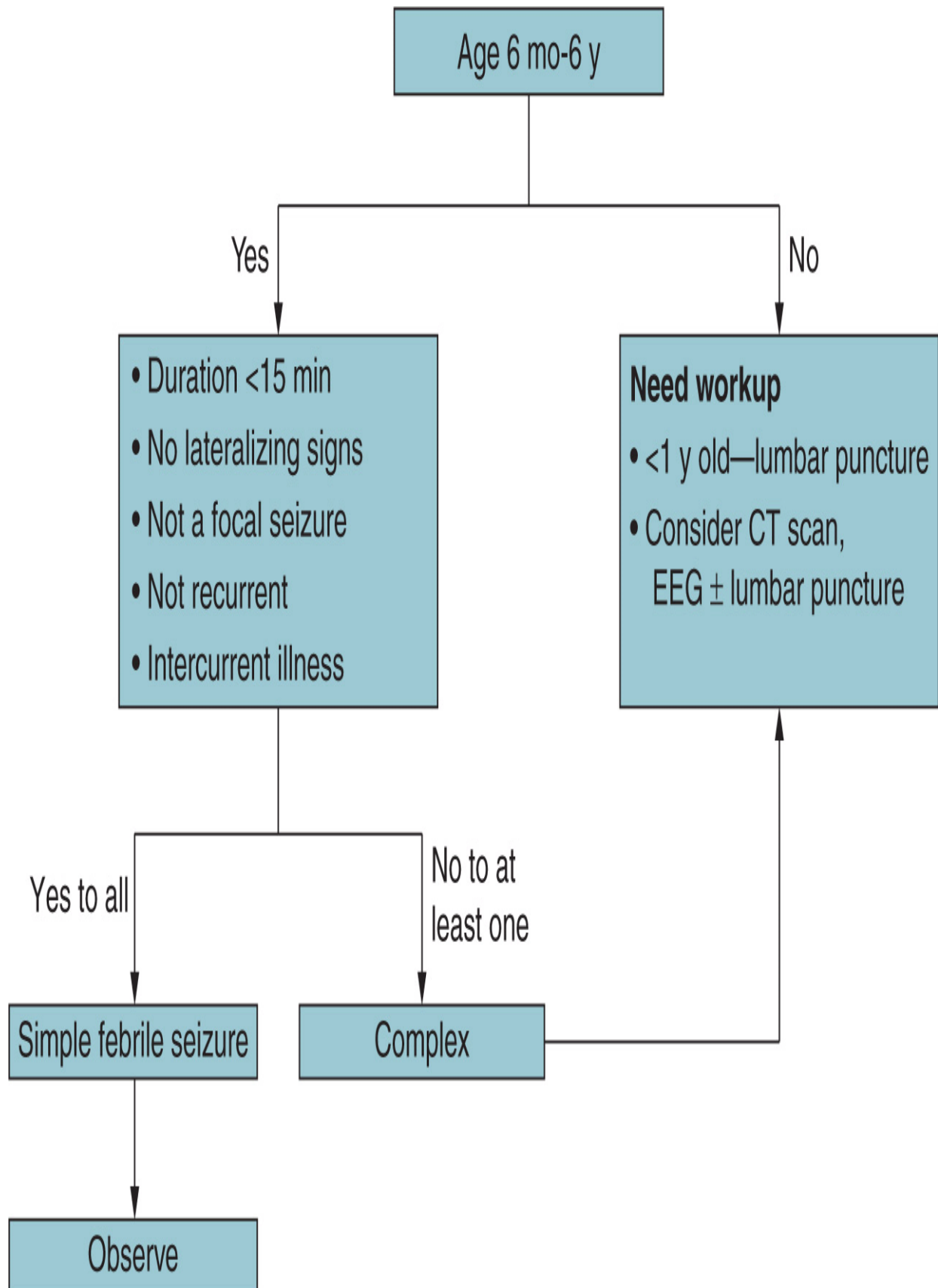
the parent but only occasionally pose a threat to the child. Febrile seizures are common, occurring in 2% to 4% of all children; they seem to have a **genetic basis** (many children have a family history of febrile seizure). Febrile seizure risk is increased (10%-20%) when a **first-degree relative** has been diagnosed with the same.

**Febrile seizures frequently are classified as simple or complex;** the distinction helps to clarify the recurrence risk and prognosis. **Simple febrile seizures last less than 15 minutes without focal or lateralizing signs or sequelae.** If more than one seizure occurs in a brief period, the total episode lasts less than 30 minutes. A complex febrile seizure lasts for more than 15 minutes and may have lateralizing signs. If several seizures occur in a brief period, the entire episode may last for more than 30 minutes.

The timing of the febrile seizure in relation to the temperature elevation is variable. Whereas many children will have a febrile seizure during the initial temperature upswing (many parents are unaware that the child is ill until the seizure and the subsequent temperature recording), some children will have seizures at other points during the febrile illness.

A febrile seizure usually is self-limited. Seizures lasting longer than 5 minutes may be interrupted with lorazepam or diazepam. Airway management is a priority, as benzodiazepines occasionally cause respiratory depression. Ongoing seizures unresponsive to lorazepam or diazepam can be interrupted with **fosphenytoin**.

The evaluation of a simple febrile seizure need not be extensive (**Figure 41-1**). Electroencephalography (EEG) is not recommended unless focal findings were present during or after the seizure, or if the seizure was prolonged. EEG is not predictive of future febrile or afebrile seizures. Laboratory studies (except as needed to determine the cause of fever) and brain imaging usually are not helpful. Imaging may be indicated for a complex febrile seizure or in patients with evidence of increased intracranial pressure. An LP is not routinely indicated, except as outlined above.



**Figure 41-1.** Algorithm for managing febrile seizures.

Prophylactic medications usually are not necessary. In the practice parameter published in 2008, the American Academy of Pediatrics emphasized that prophylactic medications for the usually benign condition of febrile seizures were not routinely useful.

**Prognosis is generally good;** most children who develop febrile seizures will not develop neurologic or developmental consequences. **Children younger than 12 months at the time of their first seizure have a 50% to 65% chance of having another febrile seizure; older children have a 20% to 30% chance of recurrence.** The chance of developing epilepsy increases from 0.5% in the general population to 1% in the child with a febrile seizure history. Children at highest risk for developing epilepsy following a febrile seizure often have preexisting neurologic problems and have complex febrile seizures; these children have 30 to 50 times the baseline risk of developing epilepsy.

## COMPREHENSION QUESTIONS

- 41.1 Paramedics bring a 7-month-old infant to the ED with seizure activity. The father reports the infant was in a normal state of health until approximately 3 days ago when she developed a febrile illness, diagnosed by her physician as a viral upper respiratory tract infection. Approximately 30 minutes ago she began having left arm jerking, which progressed to whole-body jerking. The episode spontaneously ceased on the way to the hospital. Vital signs include heart rate 90 bpm, respiratory rate 25 breaths/min, and temperature 100.4°F (38°C). Your examination reveals a sleeping infant in no respiratory distress. The child's anterior fontanelle is full. The oropharynx is clear, and crusted mucus is found in the nares. The tympanic membranes are dark and without normal landmarks. The lungs are clear, and the heart and abdominal examinations are normal. She has a bruise over the occiput and several parallel bruises along the spine. Which of the following is the best next step in management?
- A. Computed tomography (CT) of the head
  - B. Electroencephalogram (EEG)

- C. Lumbar puncture
- D. Observation
- E. Phenobarbital

41.2 A 2-year-old boy who had a simple brief febrile seizure comes to your clinic a day after his ED visit. He is currently afebrile, is happily pulling the sphygmomanometer off the wall, and is taking antibiotics for an ear infection diagnosed the previous day. His mother wants to know what to expect in the future regarding his neurologic status. You correctly tell her which of the following?

- A. He has no risk of further seizures because he was age 2 years at the time of his first febrile seizure.
- B. He will need to take anticonvulsant medications for 6 to 12 months to prevent further seizure activity.
- C. You want to schedule an EEG and a magnetic resonance scan of his head.
- D. Although he does have a risk of future febrile convulsions, seizures of his type are generally benign and he is likely to outgrow them.
- E. This is an isolated disorder, and his children will not have seizures.

41.3 A 10-month-old boy presents to the ED with a 1-day history of fever to 104°F (40°C), increased irritability, decreased breast-feeding, and refusal of solid foods. The parents brought him in after two 30-second episodes of generalized jerking that occurred over a 20-minute span. Your examination reveals an awake but lethargic infant. The anterior fontanelle is flat, the tympanic membranes and oropharynx are moist and not erythematous, the lungs are clear, and the heart and abdominal examinations are normal. He has no focal neurologic findings. Which of the following is the best next step in management?

- A. Intravenous ceftriaxone
- B. Admission overnight for observation
- C. Computed tomography of the head
- D. Discharge from ED to follow up with his primary care provider in 24 hours
- E. Lumbar puncture

- 41.4 The father of a 4-year-old girl calls your clinic to report her second febrile seizure. He states that this seizure was identical to the first one that happened 4 months ago: she developed an elevated temperature and within a short time had a generalized convulsion lasting 90 seconds. She was sleepy for approximately 2 minutes afterward. Upon awaking, she was given ibuprofen. She is now running around the house, chasing the family's chihuahua. The parents wonder if she needs to take anticonvulsants now that she has had another seizure. You should tell the father which of the following?
- A. Febrile seizures frequently are recurrent but usually have no significant long-term effect.
  - B. You will prescribe an anticonvulsant because it will reduce the risk of future epilepsy.
  - C. You will order an EEG and CT scan of her head to be done on an outpatient basis.
  - D. He needs to take his daughter to the hospital for inpatient admission.
  - E. He should stop the ibuprofen and observe the fever curve.

## ANSWERS

- 41.1 **A.** This child's history is worrisome for trauma. The fontanelle is full, bruises are found along the spine and on the occiput, and she has hemotympanum. A CT scan is of paramount importance; this child likely had a seizure from acute intracranial hemorrhage associated with physical abuse. Although this child is febrile and within the proper febrile seizure age range, the history and physical findings are more consistent with a diagnosis other than febrile seizure. Performing an LP in a patient who may have increased intracranial pressure is not advisable, an EEG would probably not reveal the diagnosis, and phenobarbital is not immediately necessary in a patient who is not actively seizing.
- 41.2 **D.** Part of the anticipatory guidance for parents of children with febrile seizures is to impress upon them that the child may have another febrile seizure; it is similarly important to emphasize the usual benign nature of this condition. In a simple febrile seizure, imaging and EEG generally are not recommended, nor are prophylactic anticonvulsants. Because febrile



seizures seem to have a genetic basis, it is possible that your patient's children will also have febrile seizures.

**41.3 E.** Although this child ultimately may be diagnosed as having had a simple febrile seizure, the patient's age (<1 year) precludes a reliable neck examination. An LP is required to evaluate the child for meningitis. Administering antibiotics before the LP (or other cultures are obtained) is inadvisable unless the patient's condition is such that he would not tolerate the procedure.

**41.4 A.** Some children will develop recurrent febrile seizures. Anticonvulsants will decrease the risk of further febrile seizures, but they do not decrease the risk of developing epilepsy. The possible adverse reactions with antiepileptic medications are numerous, including severe allergic reactions and interference with school performance; often the benefit is not worth the risk. Fever reduction with medications is generally encouraged in children with a febrile seizure history. Hospital admission and diagnostic studies are not necessary in simple febrile seizures.

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### CLINICAL PEARLS

- Febrile seizures usually are benign and self-limited. They do not require an extensive diagnostic evaluation unless they are prolonged or focal.
- A diagnosis of febrile seizure must be made only after considering the possibility of central nervous system infection as the seizure cause.
- Febrile seizures rarely lead to epilepsy; risk factors for nonfebrile seizures include preexisting developmental abnormalities and complex febrile seizures.

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## CASE 42

Parents worry about their 4-year-old son's ability to walk. He began walking at 16 months, but he was clumsy and fell frequently; they were reassured by another pediatrician that he would "outgrow it." He remains clumsier than his peers, falls during simple tasks, and has developed a "waddling" gait. Within the last month he has experienced increasing difficulty arising from a sitting position on the floor.

- What is the most likely diagnosis?

► What is the diagnostic test of choice?

► What is the mechanism of disease?

## ANSWER TO CASE 42: **Muscular Dystrophy**

*Summary:* A 4-year-old boy has delayed walking, a waddling gait, clumsiness, and proximal muscle weakness.

- **Most likely diagnosis:** Muscular dystrophy (MD), probably Duchenne type.
- **Diagnostic test:** DNA peripheral blood analysis or immunohistochemical detection of abnormal dystrophin on a muscle biopsy tissue section.
- **Mechanism of disease:** Duchenne MD is an **X-linked recessive** trait. The abnormal gene is at the Xp21.2 locus and encodes for an aberrant form of the protein dystrophin.

## ANALYSIS

### *Objectives*

1. Know the presentation of children with inherited MD.
2. Understand the inheritance pattern of the common MDs.
3. Understand the progression of the MD.

### *Considerations*

This 4-year-old boy exhibits classic Duchenne muscular dystrophy (DMD) signs: **waddling gait** and **progressive proximal muscle weakness**. Initial testing includes serum creatine kinase (CK) assessment and DNA analysis of peripheral blood for diagnosis. After the diagnosis of DMD, the family is introduced to support organizations and is offered genetic counseling. Ongoing cardiac evaluation for the development of cardiomyopathy is routine. Medical therapy is supportive.

APPROACH TO:

### **Muscular Dystrophy**

## DEFINITIONS

**GOWER SIGN:** A description of patients with proximal muscle weakness arising to a standing position. The legs are brought under the torso and weight is shifted to the hands and feet. The hands are walked toward the feet and up the thighs as the patient attempts to rise.

**TRENDELENBURG GAIT:** A pelvic waddling gait from proximal muscle weakness.

## CLINICAL APPROACH

**DMD is the most common hereditary neuromuscular degenerative disease, with an incidence of 1 in 3300 male births; 30% of cases are new mutations. It is the most severe progressive primary myopathy of childhood.**

DMD usually is asymptomatic during infancy, with normal or mildly delayed developmental milestones, but by 3 to 5 years of age patients have increasing lumbar lordosis (gluteal weakness), **frequent falling, difficulty climbing stairs, hip waddle, and proximal muscle weakness (Gower sign).** **Muscular enlargement, caused by hypertrophy of muscle fibers and infiltration of fat and collagen proliferation,** causes calf, gluteal, and deltoid muscle **pseudohypertrophy** and a “woody” feel of the affected area. Contractures of hip flexors, heel chords, and iliotibial bands develop, limiting joint range of motion. **Cardiomyopathy** with ECG findings on the precordial leads of tall R waves on the right and deep Q waves on the left can be seen. Nonprogressive intellectual impairment is common (mean IQ 80); brain atrophy can be seen on brain CT.

**Patients generally become wheelchair dependent by 10 and 13 years of age** and have rapid progression of scoliosis after the loss of ambulation. Distal muscles remain functional, permitting adequate manual dexterity. Respiratory muscle involvement and the scoliosis result in diminished pulmonary function and recurrent pulmonary infections. Oropharyngeal dysfunction can lead to aspiration, further compromising respiratory capacity.

**DNA blood analysis is diagnostic in two-thirds of cases. Muscle biopsy tissue testing** for abnormal dystrophin can be performed when blood samples are not diagnostic. Muscle biopsy findings include endomysial connective

tissue proliferation, inflammatory cell infiltrates, areas of regeneration interspersed with areas of degeneration, and areas of necrosis. Other laboratory findings include elevated CK levels. This enzyme is elevated before clinical signs (helpful in diagnosing familial cases); **in 80% of cases, female carriers have elevated CK levels.** Electromyogram findings reveal myopathy, but patients with Becker MD also have a genetic defect at the Xp21.2 locus, resulting in similar, but less severe, disease.

Treatment consists of medical therapies to slow disease progression. Orthopedic intervention, including bracing and tendon lengthening, can prolong the duration of ambulation and slow the progression of scoliosis. Caution must be exercised with surgical interventions, as these patients are prone to hyperthermia with anesthesia. Physiotherapy may delay the onset of contractures but is not intended for muscle strengthening because significant exercise can hasten muscle degeneration. The American Academy of Neurology and the Child Neurology Society recommend offering affected boys age 5 and older treatment with prednisone (optimal dosing 0.75 mg/kg/d). It is important that the potential benefits and risks of steroid therapy are discussed with the patient and family. **All DMD patients have some degree of cardiomyopathy;** it does not correlate with the degree of skeletal involvement. Thus, routine cardiac evaluation is required. Early cardiac dysfunction may be responsive to digoxin.

**Respiratory failure is often the cause of death.** Pulmonary infections are treated early and aggressively; exposure to respiratory illnesses should be limited when possible. Routine immunizations and pneumococcal vaccine are supplemented with yearly influenza vaccine.

The nutritional status of patients is monitored to ensure appropriate caloric intake. Caloric needs are lower for wheelchair-bound patients because of their decreased activity, with careful assessment for adequate intake of calcium and vitamin D; supplementation may be required to minimize osteoporosis. Patients are at risk for depression, often resulting in overeating, weight gain, and added burden to their already limited muscle function.

Another common form of MD is myotonic muscular dystrophy, the second most common type of MD in the United States. It is inherited as an autosomal dominant trait. Infants born with this condition may have an inverted V-shaped upper lip, thin cheeks, and wasting of the temporalis muscles. The head is abnormally narrow, and the palate is high and arched. In the ensuing years

weakness of the distal muscles leads to progressive challenges in walking. A variety of other findings arise including speech difficulties, gastrointestinal tract problems, endocrinopathies, immunologic deficiencies, cataracts, intellectual impairment, and cardiac involvement.

## COMPREHENSION QUESTIONS

- 42.1 The parents of a 3-year-old child are worried about the child's apparent clumsiness with frequent falls and a waddling gait. The child had normal development of motor skills during the first year of life and has normal language development. Which of the following is consistent with Duchenne muscular dystrophy?
- A. Female sex
  - B. Hypertrophy of the quadriceps
  - C. 22-year-old sister with Becker muscular dystrophy
  - D. Gower sign
  - E. Positive antinuclear antibodies in the blood
- 42.2 Which of the following is the best screening test for the child discussed in Question 42.1?
- A. Muscle biopsy
  - B. Measurement of serum creatinine
  - C. Electromyogram
  - D. Blood analysis for antinuclear antibodies
  - E. Measurement of serum creatine kinase level
- 42.3 A 12-year-old healthy boy has noticed some muscle weakness. He has experienced increasing difficulty lifting his backpack and walking long distances. He has no trouble with schoolwork, and he continues to play the piano and video games without tiring. His 38-year-old maternal uncle recently became wheelchair-bound for unclear reasons. Which of the following is the most likely diagnosis?
- A. Cerebral palsy
  - B. Duchenne muscular dystrophy
  - C. Myasthenia gravis

D. Becker muscular dystrophy

E. Guillain-Barré syndrome

42.4 A 16-year-old has just delivered a newborn through cesarean section; the delivery paperwork states the indication for the cesarean section as “ineffectual uterine contractions.” The newborn has contractures of multiple joints, facial wasting, generalized hypotonia, and weakness. The infant is transferred via helicopter to your facility. In your neonatal intensive care unit the infant’s suck is noted to be weak suggesting that gavage feeds will be required, but the child’s respiratory status worsens resulting in his requiring intubation and ventilator support. Little prenatal history is known until the great grandmother arrives. She reports the mother of the child attends special education classes and walks with braces; she knows little else since the infant’s mother only recently began to live with her. Which of the following is the likely explanation for this child’s condition?

A. Infantile botulism

B. Congenital myotonic dystrophy

C. Duchenne muscular dystrophy

D. Congenital Guillain-Barré syndrome

E. Becker muscular dystrophy

## ANSWERS

42.1 **D.** Duchenne muscular dystrophy is an X-linked recessive disease and is clinically evident only in males. Affected boys may have calf hypertrophy that occurs as a compensation for **proximal muscle weakness**. They will generally develop a Gower sign.

42.2 **E.** A definitive diagnosis can be made only using muscle biopsy tissue, but serum creatine kinase measurement is preferred because it is less invasive and results can be obtained rapidly. Electromyography will reveal nonspecific myopathy.

42.3 **D.** This patient does not have muscle weakness that precludes extended use of distal muscles (hands) or limits his manual dexterity. The child’s

presentation at age 12 years and a 38-year-old, wheelchair-bound maternal uncle suggest a diagnosis of Becker MD.

- 42.4 B. A severe, congenital form of myotonic dystrophy can be seen in infants born to mothers with myotonic dystrophy. Those that require ventilation longer than about 30 days have a poorer outcome. For none of the other entities listed would *in utero* findings be expected.

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### CLINICAL PEARLS

- Duchenne muscular dystrophy (DMD) is an X-linked recessive disorder.
  - A Gower sign reflects proximal muscle weakness and is a classic feature of DMD.
  - Creatine kinase level is elevated in patients with DMD and in many female carriers of the gene.
- 

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### CASE 43

A 10-day-old infant has a 12-hour history of fever, irritability, and decreased oral intake. She was delivered vaginally at 39-week gestation to a gravida 2, para 1 woman after an uncomplicated pregnancy with routine prenatal care. The infant went home on day 2 of life. She has surpassed her birth weight of 3.7 kg and had been well until today. On examination, she has a temperature of



101.5°F (38.6°C), and she is fussy. Her only finding on physical examination is a small cluster of 2-mm, fluid-filled lesions surrounded by an erythematous base on her parietal scalp. The infant has an episode in the emergency department of right-sided body shaking that then generalizes. The episode lasts approximately 2 minutes, and subsequently she is somnolent. Initial lumbar puncture results show 850 white blood cells with 90% lymphocytes, 200 red cells, and a protein of 200 mg/dL; a blood count reveals a platelet count of 57,000/mm<sup>3</sup>.

- ▶ What is the most likely diagnosis?
- ▶ What are the potential complications of this condition?

### ANSWERS TO CASE 43: Neonatal Herpes

*Summary:* A 10-day-old previously healthy infant with fever, irritability, decreased oral intake, and vesicles on her scalp has an episode of seizure-like activity. Laboratory studies reveal lymphocytic meningitis and thrombocytopenia.

- **Most likely diagnosis:** Neonatal herpes.
- **Potential complications of this condition:** Left untreated, the majority of infants with disseminated or central nervous system (CNS) infection die. The use of high-dose intravenous and long-duration antiviral therapy has reduced mortality and improved long-term outcomes among survivors.

## ANALYSIS

### *Objectives*

1. Recognize the importance of early recognition of neonatal herpes infection.
2. Know how to diagnose neonatal herpes infection.
3. Know the appropriate management of neonatal herpes infection.

### *Considerations*

**A young infant with fever and irritability is presumed to have a serious bacterial or viral infection.** Bacterial causes in this age include group B

*Streptococcus*, *Listeria*, and gram-negative pathogens. The history in this case of a **focal seizure**, the finding of **vesicles on the infant's scalp**, and **the laboratory findings make herpes simplex virus (HSV) the most likely pathogen**. The absence of a maternal history of herpes is not unusual; only 15% to 20% of mothers of HSV-infected infants have a history of herpes and only approximately 25% have relevant symptoms at delivery. The risk of maternal passage of HSV to the neonate is higher in cases of primary herpes outbreaks because the viral inoculum in the genital tract is high and protective antibody is not present. Most cases of transmission occur during delivery. Postpartum infection is infrequent but presents similarly. Intrauterine infection typically will cause chorioretinitis and microcephaly prior to birth.

Blood, urine, and cerebrospinal fluid (CSF) specimens are obtained for routine bacterial cultures. HSV cultures are obtained from the blood, nasopharynx, eyes, urine, stool or rectum, CSF, and from any vesicular lesion. Cerebrospinal fluid is tested by polymerase chain reaction (PCR) for HSV. A complete blood count and liver function and coagulation studies may reveal abnormalities. Pending test results, this infant is placed on intravenous antibiotics and antiviral therapy.

#### APPROACH TO:

#### **Suspected Neonatal Herpes Infection**

### **DEFINITIONS**

**NEONATE:** Infant who is 60 days old or less.

**GENITAL HERPES:** Infection of the genital tract with HSV type 1 or 2, the majority caused by HSV-2.

**PRIMARY HERPES INFECTION:** HSV infection in a previously seronegative host. Most primary infections are subclinical, but they can cause localized lesions or severe systemic symptoms.

**RECURRENT INFECTION:** Reactivation of a latent infection in an immune host. Lesions tend to be localized and are not associated with systemic symptoms.

### **CLINICAL APPROACH**

Approximately 20% to 30% of American women of childbearing age have antibodies to HSV-2, with a higher rate in women of lower socioeconomic groups and those in crowded living conditions. Approximately 75% of congenital herpes cases are caused by HSV-2. Usually HSV-2 is transmitted through sexual contact, and most genital diseases are the result of type 2 infection; HSV-1 can be transmitted sexually and occasionally is found in the genital tract. HSV-2 is associated with greater morbidity among congenital infection survivors than HSV-1.

**Cesarean delivery is generally indicated in delivering women with an outbreak of genital herpes or symptoms of HSV infection.** The infant's risk of HSV infection is increased significantly if the maternal outbreak represents **primary infection**. As many as 50% of such infants will become infected if delivered vaginally, whereas fewer than 5% will acquire the disease if the outbreak is recurrent disease. HSV surveillance cultures are not recommended in pregnant women; women at greatest risk for infecting their infants are those without prior infection history.

**Neonatal HSV disease** will present with one of the following: **localized skin, eye, and mouth involvement (SEM), or CNS disease/encephalitis, or disseminated disease with multiorgan involvement.** SEM usually presents at **1 to 2 weeks of life**; it requires **intravenous treatment to prevent progression** to one of the other presentations. **CNS disease typically occurs at 2 to 3 weeks of life.** **Fever is uncommon and only 60% of cases will have vesicles.** The infant will be lethargic, irritable, or have seizures. Recognition of the symptoms and lab findings is important as 50% of neonates without treatment will die. **Disseminated disease** has multiple signs and symptoms in the **1- to 2-week-old neonate**: fever, lethargy, irritability, anorexia, vomiting, respiratory distress, apnea, jaundice, a bulging fontanelle, seizures (focal or generalized), decerebrate posturing, or coma. **Skin vesicles** will be present in approximately two-thirds of cases. **Hepatitis, pneumonitis, shock, and disseminated intravascular coagulation (DIC)** can occur in severe cases; 30% of these neonates will not survive.

**Viral culture of samples taken from various body sites and PCR of CSF** are the most useful diagnostic tests. Serologic tests for herpes virus are not helpful in the acute setting (titers rise late in the infection's course). **Tzanck preparation** of lesions and antigen detection methods applied to the specimens can aid in **rapid diagnosis, but the sensitivity is low.** Infected

individuals often have moderate peripheral leukocytosis, elevated serum liver transaminase levels, hyperbilirubinemia, and thrombocytopenia. When the CNS is involved, the CSF frequently contains an elevated number of red cells, lymphocytes, and protein; CSF glucose usually is normal but may be reduced. Electroencephalography (EEG) shows characteristic patterns in acutely affected infants, and brain computed tomography (CT) will become abnormal as the disease progresses. HSV encephalitis in the neonatal period tends to be global, but electroencephalography (EEG) and magnetic resonance imaging (MRI) obtained in patients beyond the neonatal period may show temporal lobe abnormalities.

**Parenteral acyclovir is the preferred treatment.** It can stop the viral replication at the site of inoculation (skin, mouth, nares, eyes). Otherwise, HSV can spread in the neonate to the respiratory tract, down neurons, or enter the bloodstream, allowing hematogenous infection of the liver, adrenals, and CNS. Children with isolated skin, eye, and mouth disease generally have the best outcomes. The use of long-duration, high-dose acyclovir has reduced mortality among children with localized central nervous system disease to 4%, and to about 30% in children with disseminated disease. Most survivors of CNS disease have neurologic sequelae, but as many as 80% of survivors of disseminated infection have normal development at 12 months of age.

## COMPREHENSION QUESTIONS

- 43.1 A 10-day-old infant has a painful, red vesicular rash in the diaper area. He is mildly fussy but afebrile, and he has good oral intake. Which of the following is the most appropriate management of this infant?
- A. Hospitalize the patient, obtain HSV cultures, and initiate parenteral acyclovir.
  - B. Order an EEG and brain MRI immediately.
  - C. Perform a Tzanck smear and send the patient home if it is negative.
  - D. Prescribe an antifungal cream and follow up by telephone in 24 hours.
  - E. Schedule an appointment with a pediatric dermatologist.
- 43.2 A woman presents for her first prenatal visit at 9-week gestation. She reports that she is generally healthy, except that she has an outbreak of

genital herpes approximately once per year. To prevent transmission of the virus to her infant, her physician should do which of following?

- A. Anticipate a cesarean section delivery.
- B. Order titers to determine if the infection is HSV-1 or HSV-2.
- C. Perform weekly genital viral cultures starting at 36-week gestation.
- D. Perform a cesarean delivery if herpetic lesions or prodromal symptoms are present when labor has begun.
- E. No change in management is indicated; the risk of infant transmission is low even if she has an outbreak at delivery.

43.3 A 5-year-old with dysuria is found on examination to have herpetic genital lesions. Which of the following is the best next step in management?

- A. Ask the parent to leave the room and then ask the girl in an open-ended fashion whether she has ever been inappropriately touched in her private area.
- B. Prescribe oral acyclovir and ask her to follow up in 2 days.
- C. Admit her to the hospital for parenteral antiviral therapy.
- D. Ask how often the mother has outbreaks of genital herpes.
- E. Send a urine culture and have the mother apply petroleum jelly until the lesions heal.

43.4 The results of PCR of CSF from a 15-year-old adolescent male with encephalitis demonstrate an HSV infection. His parents ask about his prognosis. Which of the following is likely to be true?

- A. He will most likely die.
- B. He will likely survive, but will certainly have serious neurologic impairment.
- C. Most children with HSV encephalitis survive; many (but not all) are left with some permanent neurologic deficits.
- D. They should consider placing him in a long-term care facility upon discharge.

# ANSWERS

- 43.1 A. In contrast to older children and adults, neonates with suspected herpes skin lesions require parenteral antiviral therapy to prevent more serious sequelae.
- 43.2 D. Even though the viral transmission risk in the setting of a recurrent HSV outbreak is low, cesarean section is indicated if lesions are present at the time of delivery. Surveillance cultures are not recommended; negative results a few days prior to delivery do not preclude a later outbreak, and results of analysis of a more recently obtained specimen may not be available.
- 43.3 A. The possibility of sexual abuse is considered in a child who presents with genital herpes beyond the neonatal period. It is important to know who helps to bathe the child, and whether these persons have ever had herpes, as nonsexual transmission is also possible.
- 43.4 C. Although the majority of children with HSV encephalitis suffer permanent neurologic impairment, good outcomes are possible with appropriate medical and rehabilitative therapy.
- 

## CLINICAL PEARLS

- ▶ Most infants with neonatal herpes simplex virus are born to mothers without a prior history of herpes simplex virus infection.
  - ▶ The presenting signs and symptoms of neonatal herpes simplex virus may be nonspecific, without any visible herpetic lesions.
  - ▶ Neonates with suspected herpes simplex virus infection should be hospitalized for testing and parenteral antiviral therapy pending test results.
  - ▶ Neonates with herpes simplex virus skin, eye, and mouth (SEM) disease generally have the best outcomes, whereas the majority of infants with central nervous system disease develop neurologic sequelae. Approximately 30% of infants with systemic infection die despite aggressive antiviral therapy.
-

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### CASE 44

A mother brings her 11-month-old daughter to the clinic because of a persistent facial rash. The child is restless at night and scratches in her sleep. She is otherwise healthy. Physical examination reveals a well-nourished, healthy-appearing white female with dry, red, scaly areas on the cheeks, chin, and around the mouth as well as on the extensor surfaces of her extremities. The areas on the cheeks have a plaque-like, weepy appearance. The diaper area is spared. The remainder of the child's examination is normal.

- What is the most likely diagnosis?
- What is the most appropriate next step in the evaluation?
- What is the best management for this condition?

## ANSWERS TO CASE 44: Atopic Dermatitis

*Summary:* An 11-month-old female infant has dry, red, scaly areas on the extensor surfaces of her skin and on the cheeks, chin, and around the mouth, with sparing of the diaper area.

- **Most likely diagnosis:** Atopic dermatitis.
- **Next step in evaluation:** Further history to determine rash duration and exacerbating factors, and family history for atopic dermatitis, allergic rhinitis, and asthma.
- **Best management:** Topical corticosteroids, frequent use of emollients, and control pruritus.

## ANALYSIS

### *Objectives*

1. Describe incidence, etiology, and risk factors for atopic dermatitis.
2. Discuss diagnostic criteria and differential diagnoses for atopic dermatitis.
3. Describe treatment and follow-up of atopic dermatitis.
4. Be familiar with other conditions associated with atopic dermatitis.

### *Considerations*

A new rash in an infant can reflect a viral infection, as many viruses have skin manifestations. However, the lack of associated symptomatology such as fever makes infection unlikely. This child's history and examination, however, are consistent with atopic dermatitis. Further history may reveal additional risk factors for allergic disease. Treatment involves avoiding aggravating factors and ensuring intensive skin hydration.

APPROACH TO:

**Atopic Dermatitis**

## DEFINITIONS



**ATOPIC DERMATITIS (AD):** A patch or plaque of erythematous skin with intense pruritus; the most common eczematous eruption in childhood.

**CONTACT DERMATITIS:** An adverse reaction of the skin to an outside agent. Includes primary irritant dermatitis (eg, irritant diaper rash) and allergic contact dermatitis (eg, poison ivy, nickel allergy).

**ECZEMA:** General term for a skin condition consisting of acutely inflamed papules and plaques, frequently associated with serous discharge and pruritus. Eczematous eruptions include atopic dermatitis, seborrheic dermatitis, and contact dermatitis.

**EMOLLIENT:** Cream or lotion that restores water and lipids to the epidermis; those containing urea or lactic acid are more lubricating and may be more effective; creams lubricate better than lotions.

**FLEXURAL AREAS:** Areas of repeated flexion and extension, which often perspire on exertion (antecubital fossae, neck, wrists, ankles).

**LICHENIFICATION:** Epidermal thickening, with normal skin lines resembling a washboard.

**SEBORRHEIC DERMATITIS:** Self-limited scaly, erythematous, and/or crusty eruption limited to areas of the skin with a high concentration of sebaceous glands (eg, cradle cap).

## CLINICAL APPROACH

**Atopic dermatitis (eczema) typically is pruritic, recurrent, and flexural in older children and symmetrical in adults.** The term *atopy* was coined to describe a group of patients who had a personal or family history of “hay fever,” asthma, dry skin, and eczema. More than 15 million American adults and children have atopic dermatitis. The highest incidence is seen among children, and the lifetime prevalence of atopic dermatitis is 20% in children aged 3 to 11 years. Sixty-five percent of patients develop symptoms in the first year of life and 90% before the age of 5 years. The etiology is unknown, but is thought to be related to immune factors. Seventy percent of atopic patients have a family history of asthma, “hay fever,” or eczema.

**The cause of AD is thought to be multifactorial, involving genetic abnormalities of the epidermal barrier, immune function, environmental**

**exposures, and infection.** Recent studies have linked an abnormal epidermal barrier to mutations in the filaggrin (FLG) gene. Initial studies linked loss-of-function mutations of the FLG gene to ichthyosis vulgaris; more recent research, based on the known association of ichthyosis vulgaris with AD, led to evidence suggesting these same mutations are important risk factors for AD. Abnormal epidermal barrier function results in increased transepidermal fluid losses, leading to the ubiquitous finding of dry skin in AD patients. The abnormal epidermis also allows easier entrance of allergens and bacteria, stimulating an immune reaction.

Atopic dermatitis occurs in three phases: infant (**birth to 2 years**), childhood (**2 to 12 years**), and adult (**>12 years**). Infants are rarely born with atopic dermatitis, but typically develop the first signs of inflammation during the third month of life. A common scenario is a baby who, during winter months, develops dry, red, scaling cheeks without perioral and paranasal involvement. The chin is often involved; the diaper area is usually spared. The infant is uncomfortable because of intense pruritus and is often restless during sleep. Atopic dermatitis resolves in approximately 50% of infants by the age of 18 months. The most common finding in the childhood phase is inflammation in flexural areas. Perspiration stimulates burning and itching, initiating an itch–scratch cycle. Initial papules rapidly coalesce into plaques that ultimately become lichenified when scratched. The exudative lesions typical of the infant phase are not common in the childhood phase. The adult phase begins near the onset of puberty. The reason for the resurgence of inflammation may be related to hormonal changes. Adult phase disease includes flexural inflammation, often accompanied by hand dermatitis, inflammation around the eyes, and lichenification of the anogenital area. White dermographism may be seen, demonstrated by stroking the skin of a patient with AD; after the initial red line develops, a white line replaces it without wheal. Other findings include keratosis pilaris, accentuated palmar creases, small fissures at the base of the earlobe, and Dennie-Morgan creases under the lower eyelid.

Two misconceptions about atopic dermatitis are common. The first is that eczema is an emotional disorder. Patients with skin inflammation lasting for months or years are often irritable, a normal response to a frustrating disorder. The second misconception is that atopic skin disease is precipitated by an allergic reaction. Atopic individuals frequently have respiratory allergies and, when skin tested, are informed that they are “allergic to everything.”

Individuals with atopy may react with a wheal when challenged with a needle during skin testing, but this is a characteristic of atopic skin and is not necessarily an allergic response. Evidence to date indicates that most cases of atopic dermatitis are precipitated by environmental stress on genetically compromised skin and not by interaction with allergens.

### ***Patient Evaluation***

Evaluation of the child with atopic dermatitis involves ruling out other potential causes of the child's rash through a complete personal history (Table 44-1), family history, and physical examination to obtain a proper diagnosis and initiate treatment. Skin is evaluated for locations and nature of affected areas (patches, weepiness, lichenification), extent of skin dryness, and warmth or tenderness (possible secondary infection). Eyes, nose, throat, and chest are examined for evidence of allergic rhinitis or asthma (watery eyes, dark circles under eyes, runny nose, wheezing).

How long have the symptoms been present? Were there previous episodes of similar outbreaks?

How itchy are the affected areas? Is the child irritable or awakening at night because of itching and scratching?

Do symptoms appear to get worse with exposure to cold weather, wool, perspiration, or stress?

Do other family members have eczema, asthma, or allergic diseases?

Has the child had fever or other signs of infection?

**Table 44-1 • QUESTIONS TO ASK WHEN INVESTIGATING RASHES**

**Laboratory studies are not particularly helpful** in diagnosing atopic dermatitis. **A serum immunoglobulin E (IgE) level is often elevated.** Culture of the skin is performed if superinfection is suspected.

The differential diagnosis includes seborrheic dermatitis (cradle cap), which usually begins on the scalp in the first few months of life and may involve the ears, nose, eyebrows, and eyelids. The greasy brown scales of seborrheic dermatitis are in contrast to the erythematous, weeping, crusted lesions of infantile atopic dermatitis. Other considerations include scabies, irritant dermatitis (perioral fruit juice dermatitis), allergic contact dermatitis (poison ivy), and eczematoïd dermatitis (infectious lesion near a draining ear). Rare conditions might include ichthyosis, severe combined immune deficiency (SCID), Wiskott-Aldrich, zinc deficiency, drug reactions, and Letterer-Siwe disease.

### ***Treatment***

Treatment goals include preserving and restoring the skin barrier by using emollients, eliminating inflammation and infection with medications, reducing scratching through antipruritic use, and controlling exacerbating factors. Some recommend limiting bathing to brief baths or showers of moderate temperature with mild and preferably nonsoap cleansers (Cetaphil). Drying soaps (Ivory) are avoided. Lubricants (Eucerin) are applied immediately after bathing and air- or pat-drying. Some products contain urea (Nutraplus) or lactic acid (Lac-Hydrin); they have special hydrating qualities and may be more effective than other moisturizers. Lotions and creams may sting shortly after application due to bases or specific ingredients, such as lactic acid. If itching and stinging continue with each application, another product should be selected.

**Topical corticosteroids** used to control inflammation vary in potency; percentage is not an indication of potency. Lower-potency preparations (glucocorticoid groups VI and VII) can be used for longer periods to treat chronic symptoms involving the trunk and extremities. Lower-potency steroids are generally used for infants and can be added to moisturizers to cover large areas of affected skin. The lower-dose steroids have no associated adverse endocrinological side effects. Fluticasone propionate (Cutivate) is the only Food and Drug Administration (FDA)-approved topical corticosteroid cream for infants as young as 3 months. **Fluorinated corticosteroids are generally avoided on the face, genitalia, and the intertriginous area because they may depigment and thin the skin.** Higher-potency steroids (glucocorticoid groups I and II) are used only for short periods and on lichenified areas; the face and skin folds are avoided. Ointment preparations are generally

preferable because they result in better penetration of the corticosteroid, thus reducing the incidence of irritant and hypersensitivity reactions. Application is usually once to twice daily, dependent upon the preparation used. **The lowest effective potency steroid preparation should be used.** Lubrication often is continued after corticosteroids are discontinued.

Tacrolimus (Protopic) and pimecrolimus (Elidel) are nonsteroidal, immunomodulator topicals for treatment of atopic dermatitis. Tacrolimus 0.03% and pimecrolimus 1% are approved for use in children 2 years and older. These agents are recommended for short-term and long-term intermittent therapy, on a twice-daily basis, in patients not adequately responsive to, or intolerant of, conventional therapy. Neither is FDA approved for children less than 2 years of age, and both carry FDA “Black Box” warnings concerning their possible association with malignancies when used for extended periods of time. **Their exact role for use in children is under investigation; consultation with a pediatric dermatologist may be indicated.**

Oral antihistamines are used to reduce itching. Because symptoms of atopic dermatitis are often worse at night, sedating oral antihistamines (hydroxyzine, diphenhydramine) may offer an advantage over nonsedating agents. Less-sedating agents include loratadine (Claritin) and cetirizine (Zyrtec). Doxepin (Sinequan) has tricyclic antidepressant and antihistamine effects and may be useful in some cases. Topical antihistamines (Caladryl) are avoided because of the potential for skin irritation or toxicity due to absorption. Fingernails should be cut short to prevent further skin damage through scratching.

Patients with secondary bacterial infections (*Staphylococcus* or *Streptococcus* sp) often require antibiotic therapy. Topical antibiotic therapy with mupirocin (Bactroban) may be used for limited areas of infection or in the nose to reduce chronic *Staphylococcus aureus* carriage. Oral antibiotics are indicated for more extensive areas of infection. First-generation cephalosporins, erythromycin, penicillinase-resistant penicillins, or clindamycin are chosen based on local susceptibility patterns. Patients with evidence of superinfection with herpes simplex virus require oral or intravenous acyclovir.

The role of food allergies in the management of atopic dermatitis is controversial. Dietary manipulation in a child (usually less than about 3 years of age) with a strong history of exacerbation of symptoms upon exposure to a

particular food may be helpful. A 4- to 6-week trial excluding eggs and milk in children, followed by a rechallenge, may be justified, especially in a child who does not respond to first-line treatment.

Consultation with a pediatric dermatologist may be warranted for patients with an unclear diagnosis, who fail to respond to treatment, or who have extensive skin involvement. Consultation also may be appropriate for patients with ocular or serious infectious complications and for patients requiring oral steroid therapy.

**Other skin eruptions can be confused with atopic dermatitis. Contact dermatitis** is the reaction of skin to an outside agent. This category of eczematous eruptions includes both **primary irritant contact dermatitis** and **allergic contact dermatitis**. Primary irritant dermatitis can be caused by harsh detergents and soaps, bubble baths, saliva, urine, and feces. Examples of primary irritant contact dermatitis in the pediatric population include diaper dermatitis, lip-licker's dermatitis, and shin guard dermatitis seen in soccer and hockey players. Allergic contact dermatitis is a delayed T-cell hypersensitivity reaction (type IV) that occurs 7 to 14 days after initial exposure, and 1 to 4 days after subsequent exposures. The most common cause is exposure to plants of the genus *Toxicodendron* (formerly called *Rhus*) that includes poison oak, ivy, and sumac. Also common in the pediatric population is nickel allergy, causing irritation below the umbilicus where the inside of nickel-containing pant snaps rub and irritation of the earlobes in patients wearing nickel-containing earrings. Allergic contact dermatitis can also trigger an "id" reaction of widespread pruritic papules in nonexposed areas.

## COMPREHENSION QUESTIONS

- 44.1 A mother brings her 2-week-old son to the clinic for a well-baby visit. Her only concern is a rash on his face and scalp that began a week earlier. Examination reveals a healthy white male with normal vital signs and a normal examination except for yellowish, waxy-appearing, adherent plaques on the scalp, forehead, cheeks, and nasolabial folds. Which of the following therapies is appropriate for this condition?
- A. High-potency topical steroid
  - B. Topical mupirocin

- C. Phototherapy
- D. Topical ketoconazole or low-dose steroids
- E. Topical antifungal

44.2 An 8-year-old girl arrives at your clinic complaining about a minimally itchy rash on her chest, abdomen, and arms. It started with one small, scaly, red area on her chest and then spread. She is taking no medications. Physical examination reveals salmon-colored, flat, finely scaly, oval eruptions on her chest, abdomen, back, and upper arms. Which of the following is appropriate advice or therapy?

- A. Topical mupirocin
- B. High-dose topical steroid
- C. Reassurance or “supportive” therapy
- D. Three sequential weekly penicillin injections
- E. Topical antifungal

44.3 A father brings his 8-month-old daughter to an emergency room for worsening skin rash and fever. He reports that his daughter usually has weepy, red lesions on her face that are relatively well controlled with bathing her with gentle soaps, using topical emollients and steroids, and giving oral antihistamines. Over the previous few days, however, the rash has gotten progressively worse and the child has become “sicker.” Your physical examination reveals a lethargic child with an oral temperature of 103°F (39.4°C). The child’s cheeks are red and contain numerous red, punched-out, and umbilicated vesicles; some lesions are pustular. Which of the following would you prescribe?

- A. Intravenous acyclovir
- B. Prednisolone
- C. Topical bacitracin
- D. Intravenous methylprednisolone
- E. Topical acyclovir

44.4 An 8-month-old child has refractory eczema that was first noticed at 2 months of age. His past medical history reveals multiple episodes of otitis media and pneumonia, and he has now developed severe nose-

bleeds. You suspect a primary immunodeficiency. Which of the following is the next best test in your evaluation?

- A. Chromosomal analysis
- B. Chest computed tomography (CT)
- C. Complete blood count
- D. CD4 cell count
- E. Referral to ear, nose, and throat (ENT) for nasal endoscopy

## ANSWERS

- 44.1 **D.** Seborrheic dermatitis presents in infancy and adolescence. The chronic, symmetrical eruption, characterized by overproduction of sebum, affects the scalp, forehead, retroauricular region, auditory meatus, eyebrows, cheeks, and nasolabial folds. More commonly known as “cradle cap” in infants, this self-limited eruption typically develops between 2 to 3 months of age primarily on the scalp. The scale is yellow and waxy, and typically comes off with frequent shampooing. The scale may be loosened with a small amount of oil. In infants who do not respond to shampooing with baby shampoo, an antidandruff shampoo containing antifungal medication (Nizoral) or selenium may help, as will low-to medium-potency topical corticosteroids.
- 44.2 **C.** Pityriasis rosea is preceded by a “herald patch,” an annular, scaly, erythematous lesion. The lesions are salmon-colored and in a Christmas-tree formation, following the lines of the skin. The cause is unknown. Treatment may include antihistamines, topical antipruritic lotions and creams, low-dose topical corticosteroids, and phototherapy. The rash usually lasts up to 6 weeks and then resolves. It can be confused with nummular eczema and tinea versicolor. In the sexually active adolescent, syphilis should also be considered.
- 44.3 **A.** Atopic infants may develop rapid onset of diffuse cutaneous herpes simplex. The disease is most common in areas of active or recently healed atopic dermatitis, particularly the face. High fever and adenopathy occur 2 to 3 days after the onset of vesiculation. Viral septicemia can be fatal. Eczema herpeticum of the young infant is a medical emergency. The child should be admitted immediately for intravenous acyclovir.



44.4 C. This patient most likely has Wiskott-Aldrich syndrome, an X-linked condition with recurrent infections, thrombocytopenia, and eczema. Infections and bleeding usually are noted in the first 6 months of life. Potential infections include otitis media and pneumonia caused by poor antibody response to capsular polysaccharides, and fungal and viral septicemias caused by T-cell dysfunction. A complete blood count could aid diagnosis; thrombocytopenia usually is in the 15,000 to 30,000/mm<sup>3</sup> range, and platelets are typically small. In addition to eczema, these children have autoimmune disorders and a high incidence of lymphoma and other malignancies.

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### CLINICAL PEARLS

- Atopic dermatitis is a chronic, itchy disease that often begins in childhood. In infancy, the itchy eruption is found on the face and cheeks; by childhood, the rash is noted in flexural areas.
  - Baseline therapy for atopic dermatitis is avoidance of drying soaps and replenishment of skin hydration with emollients; topical steroids may be required.
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## CASE 45

A father reports his 3-year-old daughter has decreased energy, loss of appetite, and an enlarging abdomen over the past few weeks. Intermittent emesis began yesterday. Physical examination reveals pallor, proptosis, periorbital discoloration, and a large, irregular abdominal mass along her left flank that crosses the midline. Her vital signs and the remainder of her examination are normal.

- ▶ What is the most likely diagnosis?
- ▶ What is the next step in evaluation?

### ANSWERS TO CASE 45: **Neuroblastoma**

*Summary:* A toddler with fatigue, decreased appetite, periorbital discoloration, and a multiquadrant abdominal mass.

- **Most likely diagnosis:** Neuroblastoma.
- **Next step in evaluation:** Select laboratory testing and imaging to ascertain tumor genetic characteristics, location and extent, and impact on surrounding structures. Resultant staging and risk stratification help guide decision-making regarding perisurgical chemotherapy and/or irradiation.

## ANALYSIS

### *Objectives*

1. Recognize the signs and symptoms of neuroblastoma.
2. Describe the diagnosis and treatment of neuroblastoma.

### *Considerations*

Since neuroblastoma origin and progression vary from patient to patient and a mass may not always be readily apparent on examination, clinicians must

perform thorough histories and comprehensive examinations to ensure timely and accurate diagnosis and diminish the potential for metastatic disease at discovery. The diagnostic evaluation includes questioning and examining for syndromes associated with neuroblastoma.

APPROACH TO:

**Suspected Neuroblastoma**

## DEFINITIONS

**HORNER SYNDROME:** Characterized by eyelid ptosis and sluggish pupillary reflex; related to sympathetic nervous system dysfunction.

**PARANEOPLASTIC SYNDROME:** Characterized by hypertension and secretory diarrhea; related to tumor production of catecholamines and vasoactive intestinal peptide.

**OPSOCLONUS-MYOCLONUS SYNDROME:** Characterized by chaotic eye movements and myoclonic jerks; described as “dancing eyes, dancing feet” related to autoantibodies produced against neuronal elements.

## CLINICAL APPROACH

Neuroblastoma is comprised of primitive neuroendocrine tissue. Its etiology is poorly understood, but believed to be multifactorial. It is the most prevalent solid, extracranial tumor in children and accounts for more than half of all cancers in infancy. Most arise in the abdomen from the adrenal gland, with other origins including intrathoracic and paraspinal neuronal ganglia.

Signs and symptoms related to neuroblastoma depend on tumor location; cervical ganglia tumors may cause Horner syndrome, intrathoracic tumors (most commonly seen in infancy) may be associated with wheezing and respiratory distress, and paraspinal tumors may cause compressive neuralgias, back pain, and urinary or stool retention. Abdominal masses are typically nontender, irregular, and cross the midline. Dependent on a tumor's location and impact on surrounding structures, intrathoracic or paraspinal decompressive surgery may emergently be required.

Metastatic disease typically involves the skin, lungs, liver, and bone. Bluish skin discoloration (most often seen in infancy) represents subcutaneous infiltration. Pulmonary involvement can promote increased work of breathing, dyspnea, and pneumonia. Bone marrow infiltration may cause bone pain and pancytopenia; petechiae, bruising, pallor, and fatigue may occur. If the orbital bones are involved, proptosis and bluish periorbital discoloration, described as “raccoon eyes,” may be noted. Generalized lymphadenopathy also is common. Some patients develop paraneoplastic syndrome related to tumor neuroendocrine mediators, or opsoclonus-myoclonus syndrome (an autoimmune-mediated phenomenon that may be characterized by cerebellar ataxia).

The major differential diagnostic consideration is Wilms tumor. These tumors typically are associated with hematuria, hypertension, and a localized abdominal mass that rarely crosses the midline. In general, patients with neuroblastoma are slightly younger and sicker than patients with Wilms tumor.

Computed tomography (CT) or magnetic resonance imaging (MRI) is useful in identifying and assessing the extent of neuroblastoma. Laboratory markers include **elevated urinary vanillylmandelic acid and homovanillic acid levels (catecholamine metabolites), observed in approximately 90% of neuroblastoma patients**; other markers include elevated enolase, ferritin, and lactate dehydrogenase levels.

Treatment involves surgical excision of the tumor, usually after chemotherapy and/or radiotherapy to decrease tumor size. Combined multi-agent chemotherapy and radiotherapy often is used in patients with advanced-stage neuroblastoma. Staging is classically dependent on tumor location and extent, with risk assessment and therapeutic decision-making based on variables such as age at diagnosis and staging (eg, stage 2 disease localized to the abdomen of a 1-year-old requiring only limited postexcision chemotherapy versus stage 4 disease with bony metastases in a toddler mandating multi-agent chemotherapy and bone marrow transplantation). Other therapies under investigation include monoclonal antibody immunotherapy and radionuclide therapy.

Overall cure rates for neuroblastoma can exceed 90%, **with infants typically having a better prognosis than older children**. Select features, such as skeletal metastases or *N-myc* oncogene amplification at the cellular level, often denote a poor prognosis.

## COMPREHENSION QUESTIONS

- 45.1 A mother recently feels a mass in the abdomen of her 4-year-old son during a bath, and brings him to your clinic for evaluation. He has no history of emesis, abnormal stooling, or abdominal pain. Physical examination reveals a resting blood pressure of 130/88 mm Hg, heart rate of 82 beats/minute, pallor, and a firm left-sided abdominal mass that doesn't cross the midline. Which of the following is the most likely explanation for these findings?
- A. Constipation
  - B. Intussusception
  - C. Neuroblastoma
  - D. Wilms tumor
  - E. Volvulus
- 45.2 A 1-week-old infant presents with a right midquadrant abdominal mass and decreased urinary output. There has been no temperature lability, irritability, or abnormal stooling or urine appearance. Which of the following tests would be most helpful in determining the etiology of this infant's abdominal mass?
- A. Complete blood count
  - B. Abdominal ultrasound
  - C. Urinary catecholamines
  - D. Abdominal computed tomography (CT)
  - E. Barium enema
- 45.3 A father presents his otherwise healthy 15-month-old daughter to the emergency center with cough, post-tussive emesis, and subjective fever over the past 3 days. He also thinks her abdomen has been hurting her. Diarrhea started yesterday, with "regular" stooling prior to this illness. She has been drinking well and recently had a wet diaper. Physical examination reveals normal vital signs, congested nares, shoddy neck lymphadenopathy, and a mildly distended and apparently tender abdomen without obvious guarding. Which of the following is the next best step in your evaluation?

- A. Obtain abdominal computed tomography (CT)
  - B. Biopsy lymph node
  - C. Collect 24-hour urine for catecholamines
  - D. Admit to the hospital for exploratory laparotomy
  - E. Reassure parent and await spontaneous resolution
- 45.4 During a routine preventive health visit for a 3-year-old boy, you incidentally note an irregular abdominal mass involving both lower quadrants. His mother denies having noted this previously and declares her son to be generally healthy. There has been neither gastrointestinal distress nor apparent abdominal pain. Beyond the abdominal mass and pallorous conjunctivae, his vital signs and physical examination are normal. Which of the following tests would be most helpful in determining the etiology of his abdominal mass?
- A. Abdominal radiograph
  - B. Chest radiograph
  - C. Urinary catecholamines
  - D. Complete blood count
  - E. Urine myoglobin

## ANSWERS

- 45.1 **D.** The scenario presented is typical for Wilms tumor. Beyond abdominal imaging, checking a urinalysis for hematuria, metabolic panel for renal or hepatic dysfunction, and complete blood count for anemia should be considered in the workup of Wilms tumor.
- 45.2 **B.** This infant most likely has a urinary tract obstruction. In the newborn, a palpable abdominal mass is commonly a hydronephrotic or multicystic dys-plastic kidney, and typically can be easily identified by ultrasound.
- 45.3 **E.** Upper respiratory tract infection symptoms, neck lymphadenopathy, and diarrhea are consistent with viremia; viral-mediated mesenteric lymph node enlargement can occur and cause nonspecific abdominal pain. Parental reassurance is adequate in this otherwise healthy child with classic viremia signs. An abdominal CT scan may show diffuse,

mildly enlarged lymph nodes in mesenteric lymphadenitis, but imaging is rarely warranted unless an etiology for abdominal pain remains elusive.

- 45.4 C. This boy's history and examination are consistent with neuroblastoma. Given the vast majority of neuroblastoma patients have elevated urinary catecholamines, a 24-hour quantitative assessment of these metabolites should be confirmatory.
- 

### CLINICAL PEARLS

- Neuroblastoma may present with an abdominal mass, pallor, proptosis, and "raccoon eyes."
  - Masses are often discovered incidentally by a family member or on routine physical examination.
  - Patients with neuroblastoma are slightly younger and appear sicker than patients with Wilms tumor.
  - Approximately 90% of neuroblastoma patients have elevated levels of the catecholamine metabolites, vanillylmandelic acid and homovanillic acid.
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A mother reports that her 4-year-old daughter complains of sore throat and difficulty swallowing for 3 days. She has been irritable and does not want to move her neck. Her appetite and intake have decreased, and she has vomited twice overnight. She exhibits no symptoms of upper respiratory tract infection (URI). She is otherwise healthy with up-to-date immunizations. Her physical examination is remarkable for fever to 102°F (38.9°C), bilateral tonsillar exudates, and an erythematous posterior oropharynx with right posterior pharyngeal wall swelling.

- ▶ What is the most likely diagnosis?
- ▶ What is the most appropriate next step in the evaluation?

### ANSWERS TO CASE 46: **Retropharyngeal Abscess**

*Summary:* An ill-appearing toddler with sore throat, odynophagia, fever, and an abnormal oropharyngeal examination.

- **Most likely diagnosis:** Retropharyngeal abscess.
- **Next step in evaluation:** Laboratory testing might include group A beta-hemolytic *Streptococcus* (GAS) immunoassay and culture. Radiologic evaluation might include lateral cervical x-ray and computed tomography (CT) or magnetic resonance imaging (MRI) to elucidate location and extent of infection.

## ANALYSIS

### *Objectives*

1. Discuss the diagnosis and treatment of retropharyngeal abscess.
2. Differentiate between various forms of neck abscess.
3. Discuss neck conditions presenting similarly to retropharyngeal abscess.

### *Considerations*

History and examination for this toddler with odynophagia, fever, and posterior pharyngeal swelling is consistent with retropharyngeal abscess. Because a variety of head and neck lesions can present similarly, the



diagnostic challenge lies in determining whether a bacterial infection is present, the extent of infection, the possible need for surgical intervention, and whether the potential exists for spread to surrounding vital structures.

APPROACH TO:

**Retropharyngeal Abscess**

## DEFINITIONS

**RETROPHARYNGEAL SPACE:** Bordered by layers of the deep cervical fascia; located posterior to the esophagus; contains lymphatics draining the middle ears, sinuses, and nasopharynx; contiguous with the posterior mediastinum.

**PARAPHARYNGEAL (LATERAL) SPACE:** Comprises anterior and posterior compartments containing lymph nodes, cranial nerves, and carotid sheaths; infections in the lateral space can originate from the oropharynx, middle ears, and teeth.

**PERITONSILLAR SPACE:** Bordered by tonsils and pharyngeal musculature; peritonsillar abscess is typically an extension of acute tonsillitis.

**EPIGLOTTITIS:** Infection of the cartilaginous structure protecting the airway during swallowing; bacterial etiology (classically *Haemophilus influenzae*) requiring intravenous antibiotics; fever, drooling, and toxicity are common; emergent airway obstruction is possible.

**RAPID STREP IMMUNOASSAY:** Detects GAS antigen by latex agglutination or enzyme-linked immunosorbent assay; high specificity and variable sensitivity with false-negative results possible.

**MONOSPOT:** Latex agglutination of heterophile antibodies to erythrocytes in Epstein-Barr virus (EBV) infection; high specificity and sensitivity in patients older than 3 years; infection may be confirmed by EBV immunoglobulin (Ig)M antibody if heterophile negative.

**STRIDOR:** Abnormal, musical breathing as a result of large airway obstruction. **DYSPHAGIA:** Difficulty swallowing.

**ODYNOPHAGIA:** Pain on swallowing.

**TRISMUS:** Inability to open the mouth secondary to pain or inflammation or mass effect involving facial neuromusculature.

## CLINICAL APPROACH

**Categorization of deep neck infections** is based on a combination of **examination findings** and **neck imaging**. The type and extent of infection ultimately determine whether a patient requires surgery and could be at risk for infection of nearby vital structures, including the mediastinum. Multiple compartments exist within the neck, bordered by musculature and fascia and containing various neurovascular structures (cranial nerves and carotid arteries); infections can easily spread along these fascial planes.

Some age predilections are noted in neck abscess. The typical pediatric patient with **retropharyngeal abscess**, for example, is a **toddler younger than 4 years**, coinciding with the time when the majority of URI and otitis cases are seen. **Peritonsillar abscess** can be seen at any age, but **prevalence is greater in the adolescent or young adult**. Of all abscess types, **peritonsillar abscess is the most common type in the pediatric population**.

Infections of the various neck spaces may present similarly. Fever, irritability, and toxicity are common, with patients usually complaining of sore throat, dysphagia, odynophagia, or trismus, with trismus noted more frequently with peritonsillar or parapharyngeal infection.  **Drooling and increased work of breathing or frank stridor** also can be seen. On examination, neck lymphadenopathy is noted more often in patients with peritonsillar or parapharyngeal abscess. Peritonsillar or soft palatal swelling is more prominent with peritonsillar abscess. A patient who **passively refuses to move the neck secondary to pain is likely to have retropharyngeal infection**.

Imaging in the patient with suspected neck abscess starts with a **lateral cervical x-ray**. Radiographic evidence for retropharyngeal abscess on a lateral film includes widening of the retropharyngeal space. Findings on a lateral film in a patient with sore throat and fever may lead to an alternative diagnosis, as in the patient with epiglottic edema and **classic “thumb sign” in epiglottitis**. Cervical CT imaging is an excellent study for determining whether a patient has only cellulitis and edema surrounding a space, or hypodensity and rim enhancement consistent with an abscess. It also

delineates whether there has been extension to contiguous structures. An MRI is an alternative when there is a concern for infection involving a compartment with neurovascular elements and more accurate visualization is desired.

Specific neck space infections have specific origins and complications. Infections involving the teeth, ears, and sinuses may spread to the parapharyngeal space, and may ultimately **impact neurovascular elements in the lateral space**, either because of erosion or mass effect. Lymph chains draining the sinuses and oropharynx can seed the retropharyngeal space, with potential for spread to the mediastinum, where impact on cardiorespiratory function or mediastinitis could develop. An infection in one compartment can always spread to another. Generally, a neck abscess results when there is contiguous spread of bacteria in a patient with pharyngitis, odontogenic infection, otitis, mastoiditis, sinusitis, or other head and neck infection.

Bacterial etiologies for neck abscess include *Streptococcus pyogenes*, *Staphylococcus* sp, *Haemophilus influenzae*, *Peptostreptococcus* sp, *Bacteroides* sp, and *Fusobacterium* sp. Polymicrobial infection is typically seen, often reflective of the organisms most commonly found in infections involving the oropharynx, ear, or sinuses.

Viral etiologies include EBV, cytomegalovirus, adenovirus, and rhinovirus and may present similarly to bacterial infection. Viruses can present with oropharyngeal exudate and swelling or neck masses in the form of lymphadenopathy. A viral process usually can be differentiated from a more concerning bacterial process by ancillary testing previously described and taking into consideration symptomatology more frequently seen in viremia. For example, an exudative pharyngitis with neck findings, rhinorrhea, and cough is more consistent with viral infection.

Standard therapies include intravenous penicillins, advanced-generation cephalosporins, or carbapenems. Clindamycin or metronidazole is added if anaerobes are suspected and broad coverage is desired. Clindamycin often is a good choice for monotherapy in the patient with penicillin allergy. Broad-spectrum antibiotics are started in the patient with neck abscess, with treatment modification if an organism is identified from oropharyngeal or surgical samples. Ultimately, pediatricians and surgeons determine whether to pursue a “watchful waiting” approach with a patient taking antibiotics, or to proceed quickly with needle aspiration or incision and drainage based on

infection extent, current impact on surrounding structures, and expectations for progression.

Other abnormalities, unrelated to deep neck infection, also can cause sore throat, odynophagia, or swelling and pain of the oropharynx or neck. They include anatomic variants such as thyroglossal duct cyst or second branchial cleft cyst. Arising from vestigial structures, these cysts can become secondarily infected and develop overlying tenderness and erythema that might be confused with deeper infection. Thyroiditis and sialadenitis also present with fairly localized neck findings. Depending on location, one also should consider thyroid nodule, goiter, or salivary gland tumor, particularly in the case of an initially nontender mass that grows slowly.

## COMPREHENSION QUESTIONS

- 46.1 A mother notices a lump on her 5-year-old son's neck. He complains about pain in the region and difficulty swallowing. Appetite and intake are normal. On examination, he is afebrile with a 3-cm × 3-cm area of mild erythema, fluctuance, and tenderness of the central anterior neck. The mass moves superiorly when he opens his mouth. His oropharynx is clear. Which of the following symptoms was most likely present during the preceding week?
- A. Diarrhea
  - B. Abdominal pain
  - C. Dizziness
  - D. Urinary frequency
  - E. Cough
- 46.2 A 9-year-old girl complains of sore throat and anterior neck pain of 1-day duration, and nasal congestion and cough over the past 3 days. There has been no nausea or change in appetite. She describes "lumps growing in her neck" over the past day. Her past medical history is unremarkable. She is afebrile with a clear posterior oropharynx and a supple neck. She has four firm, fixed, and minimally tender submandibular masses without overlying skin changes; the largest mass is 1 cm in diameter. Which of the following is the most likely explanation for these findings?
- A. Lymphadenopathy

- B. Peritonsillar abscess
- C. Retropharyngeal abscess
- D. Sialadenitis
- E. Streptococcal pharyngitis

46.3 A father states that his 7-year-old daughter has a 1-week history of mouth and neck pain. She describes pain on chewing and swallowing. Slight swelling around her right, lower jaw was first noted yesterday. She has been afebrile and exhibits no URI symptoms. Her examination reveals a temperature of 100.22° (37.9°C) with swelling, tenderness, and warmth overlying the right, posterior mandible without fluctuance or skin changes. Scattered, bilateral neck lymphadenopathy is appreciated. Her posterior oropharynx is minimally erythematous, with marked swelling and tenderness of the gum surrounding the posterior molars of the right mandible. Which of the following is the most appropriate next step?

- A. Admit her immediately to the hospital for intravenous antibiotics.
- B. Commence a broad-spectrum antibiotic and advise her to see a dentist as soon as possible.
- C. Obtain an immediate surgery consult.
- D. Order a cervical CT and obtain ear, nose, and throat (ENT) consultation today.
- E. Perform a rapid strep immunoassay in your clinic.

46.4 A previously healthy, 4-year-old boy has been febrile for a day. He does not want to drink and vomited this morning. There have been no URI symptoms or diarrhea. On examination, he is sleepy, but arousable, and has a temperature of 102.8°F (39.3°C). His posterior oropharynx is markedly erythematous with enlarged, symmetrical, and cryptic tonsils that are laden with exudate. Shoddy cervical lymphadenopathy is noted. He moves his head vigorously in an effort to thwart your examination. Which of the following is the next best step in your evaluation?

- A. Lumbar puncture
- B. Cervical CT
- C. Tonsillar needle aspiration
- D. Rapid streptococcal testing

E. Complete blood count

## ANSWERS

- 46.1 E. Thyroglossal duct cysts, arising from the embryonic thyroglossal tract, are typically midline, often move on tongue protrusion, and often are noted after a URI. Treatment is usually surgical excision, sometimes after neck CT imaging to ascertain cyst and thyroid anatomy. About half can become infected.
- 46.2 A. This patient has viral URI symptoms, most likely causing reactive lymph-adenopathy. Supportive care such as analgesics would be a reasonable treatment recommendation. Rapid streptococcal testing usually is not warranted for classic URI symptoms; streptococcal pharyngitis more commonly presents with sore throat, headache, nausea, and/or fever. Signs of viremia and her neck examination do not suggest sialadenitis or neck abscess.
- 46.3 B. Tooth abscess is her most likely diagnosis, as evidenced by obvious gingival inflammation and other signs of ongoing infection in the area, despite the absence of frank pus from an evident cavity. Potential causative organisms include *Streptococcus mutans* and *Fusobacterium nucleatum*. Therapy includes an antibiotic (amoxicillin or clindamycin) and referral to her dentist within the next 24 hours. Deep neck infection is unlikely; imaging and IV antibiotics are not warranted at this time.
- 46.4 D. This child has a fairly classic examination for streptococcal tonsillitis. The potential for a retropharyngeal or peritonsillar process is diminished by the lack of tonsillar asymmetry, soft palatal changes, and nuchal rigidity. A rapid streptococcal immunoassay would be a good initial test; a swab for culture may be sent as well. Standard therapy would include oral or intramuscular penicillin in the nonallergic patient and an analgesic/antipyretic. If the streptococcal immunoassay is negative, some treat patients whose history and examination are consistent with streptococcal infection while awaiting culture.

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## CLINICAL PEARLS

- Infections involving specific compartments of the neck have specific complications, such as the potential for mediastinitis in the patient with retropharyngeal abscess.
  - Multiple bacterial and viral etiologies, including GAS and EBV, are possible in the patient with constitutional symptoms and neck findings. Extension of these infections into cervical compartments may endanger surrounding vital structures and potentially require surgery.
  - Various head and neck abnormalities (infected thyroglossal duct cyst or extensive reactive lymphadenopathy) may mimic deep neck infection.
- 

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A term 3700-g male infant is born vaginally to a 27-year-old gravida 2 mother following an uncomplicated pregnancy. Shortly after birth, he begins to cough, followed by a choking episode, difficulty handling secretions, and cyanosis. During the resuscitation, placement of an orogastric tube meets resistance at 10 cm. He is transferred to the level II nursery for evaluation and management of respiratory distress.

- ▶ What is the most likely diagnosis?
- ▶ What is the best test for evaluation?

### ANSWERS TO CASE 47: Esophageal Atresia

*Summary:* A newborn with cough, choking, cyanosis, and inability to undergo passage of an orogastric tube.

- **Most likely diagnosis:** Esophageal atresia, probably with a tracheoesophageal fistula (TEF).
- **Best test for diagnosis:** A chest and abdomen radiograph with the orogastric tube in place will demonstrate a coiled tube in the esophageal blind pouch.

## ANALYSIS

### *Objectives*

1. Become familiar with the presentation of TEF.
2. Understand the anatomic variants of TEF.
3. Understand emergency management of newborns with TEF.

### *Considerations*

In this newborn with choking and coughing, esophageal atresia is suspected when an orogastric tube does not pass. Infants with esophageal atresia cannot handle oral secretions and require constant esophageal pouch drainage to



prevent aspiration. They are monitored in the neonatal intensive care unit while awaiting surgical intervention.

APPROACH TO:

**Esophageal Atresia**

## DEFINITIONS

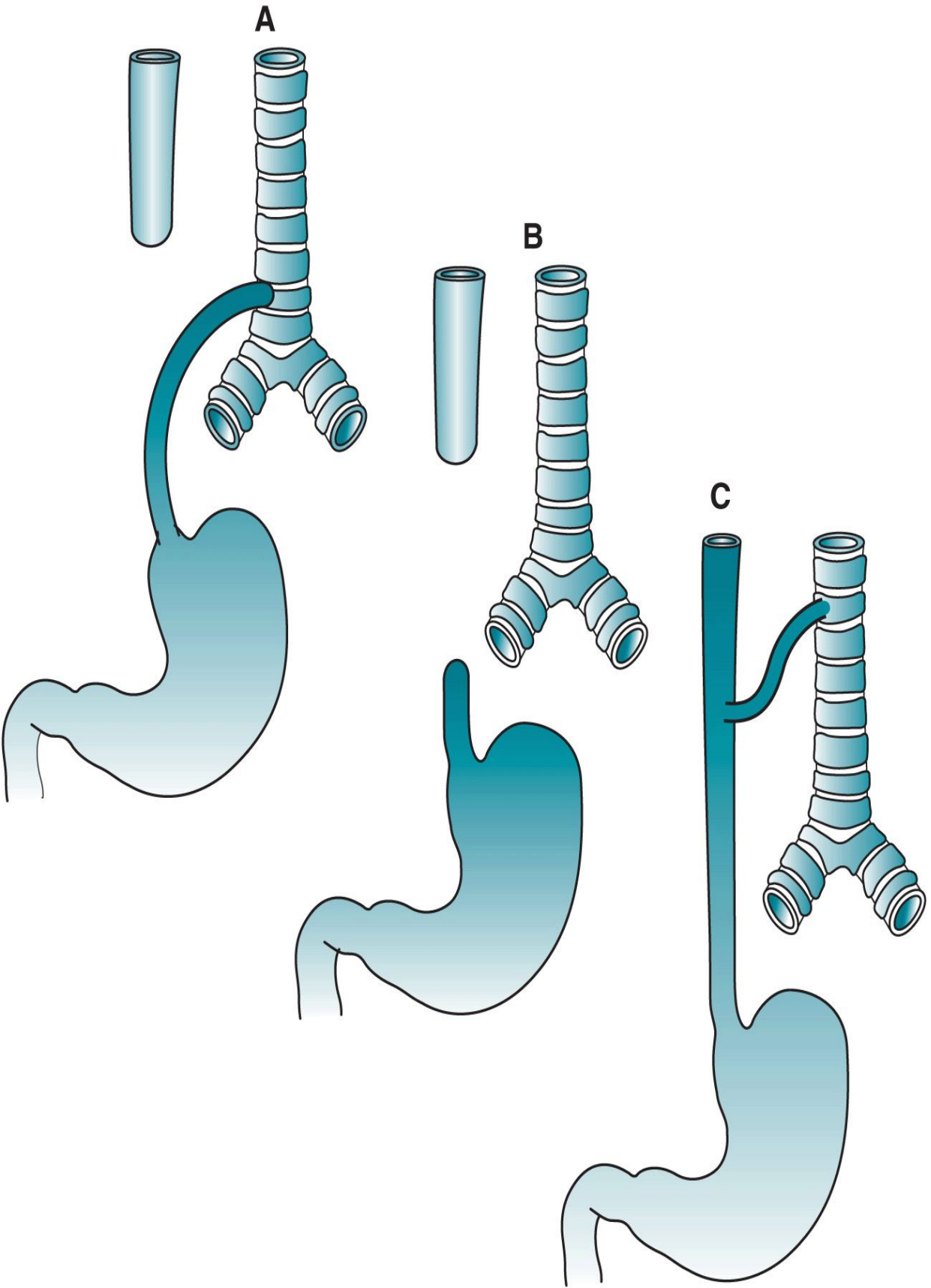
**ASSOCIATION:** Sporadic occurrence of two or more clinical features occurring together more commonly than would be expected, but without an identifiable cause.

**POLYHYDRAMNIOS:** Diagnosis of an increased amount of amniotic fluid.

**SYNDROME:** A constellation of features having a common cause (such as the features of Down syndrome being caused by a trisomy 21).

## CLINICAL APPROACH

Esophageal atresia occurs in 1 in 2500-3000 live births, usually accompanied by TEF. Polyhydramnios, which is also seen in duodenal atresia, is a common pregnancy complication seen with TEF. Five different TEF anatomic variants occur; the most common (87%) includes proximal atresia (esophageal pouch) with a distal fistula ([Figure 47-1](#)).



**Figure 47-1.** Types of esophageal atresia/tracheoesophageal fistula. **A.** Proximal esophageal atresia with distal fistula (80%-90%). **B.** Esophageal atresia (10%). **C.** H-type tracheoesophageal fistula (3%).

Infants with TEF usually present in the newborn period with excessive oral secretions and coughing, choking, and cyanosis secondary to aspirated secretions or with initial feeds. Infants with the **“H-type” fistula** (approximately 4% of cases) often present later in life with recurrent aspiration pneumonia or feeding difficulty. Other congenital anomalies occur in approximately 30% to 50% of TEF patients, and a search for them is undertaken. The most common association is the **VATER association**(vertebral abnormality, anal imperforation, tracheoesophageal fistula, radial and renal anomaly).

Neonates with TEF or esophageal atresia are at risk for respiratory compromise due to aspiration. The esophageal pouch requires constant suctioning while awaiting surgery to ligate the fistula and anastomose the esophagus. Staged surgery is required if anatomic conditions preclude primary anastomosis. Postsurgical esophageal dysmotility may persist; chronic gastroesophageal reflux is common.

## COMPREHENSION QUESTIONS

- 47.1 A 2-hour-old term newborn male has coughing, choking, and cyanosis prior to feeding. A nasogastric tube is placed and meets resistance at 10 cm. Prenatal history is significant for polyhydramnios. Which of the following is most likely to be found in this infant?
- A. Congenital cataracts
  - B. Gingival hyperplasia
  - C. Hepatosplenomegaly
  - D. Microcephaly
  - E. Fusion of two lower thoracic vertebral bodies
- 47.2 An infant with a history of recurrent pneumonia is diagnosed with TEF at 8 months of age. Which of the following statements is correct?
- A. The infant most likely has an “H-type” TEF.

- B. The infant most likely has proximal esophageal atresia with distal fistula.
  - C. The infant likely has a previously undetected, associated finding of imperforate anus.
  - D. The infant is unlikely to have gastroesophageal reflux.
  - E. The infant is likely to have cystic fibrosis.
- 47.3 A 2-year-old girl with a history of esophageal atresia and a ventricular septal defect is hospitalized with *Pneumocystis carinii* pneumonia. Her immunodeficiency is likely a result of which of the following?
- A. Bruton agammaglobulinemia
  - B. Chronic granulomatous disease
  - C. DiGeorge syndrome
  - D. Hyperimmunoglobulin E syndrome
  - E. Severe combined immunodeficiency syndrome
- 47.4 A 2-year-old boy, living with new foster parents for 3 weeks, has become progressively short of breath. When he first arrived at their home, he was active and playful, but now he is too tired to play. They have few details, but they know that he had neonatal surgery for a problem with his “esophagus being connected to his lungs” and that he takes no medications. On examination, he is afebrile, diaphoretic, tachycardic, and tachypneic. His symptoms can most likely be attributed to which of the following?
- A. Adjustment disorder
  - B. Heart failure secondary to ventricular septal defect
  - C. Kawasaki disease
  - D. Reactive airway disease
  - E. Rheumatic heart disease

## ANSWERS

- 47.1 E. The infant probably has esophageal atresia. VATER association, as described in the case, can have vertebral anomalies such as fused or bifid

vertebral bodies. None of the other findings listed is commonly associated with VATER.

- 47.2 **A.** This infant likely has an H-type TEF, found later in infancy with recurrent pneumonias and/or feeding difficulty. Patients with esophageal atresia and distal fistula present in the first hours of life because of their inability to swallow oropharyngeal secretions. Infants with imperforate anus also present as neonates. All patients with TEF are at high risk for gastroesophageal reflux.
- 47.3 **C.** DiGeorge syndrome (thymic hypoplasia) results from abnormal third and fourth pharyngeal pouch formation during fetal development. Neighboring structures formed during the same fetal growth period are often affected. Associated conditions include anomalies of the great vessels, esophageal atresia, bifid uvula, congenital heart disease, short philtrum, hypertelorism, antimongoloid slant palpebrae, mandibular hypoplasia, and low-set, notched ears. DiGeorge syndrome may present in neonates as hypocalcemic seizures because of parathyroid hypoplasia.
- 47.4 **B.** This child likely had undergone TEF repair and has associated congenital heart disease with heart failure symptoms.

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### CLINICAL PEARLS

- VATER association, vertebral (abnormality), anal (imperforation), tracheoesophageal (fistula), radial and renal (anomaly), is often seen in patients with tracheoesophageal fistula.
  - Esophageal atresia is associated with DiGeorge syndrome.
  - The H-type tracheoesophageal fistula often presents later in infancy as recurrent pneumonitis and can be difficult to diagnose.
- 

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## CASE 48

A term male is born at 38 weeks through a scheduled repeat cesarean section prior to the onset of labor. The infant's mother had good prenatal care including vaginal cultures negative for group B *Streptococcus*. At the delivery, the amniotic fluid was clear and was not foul-smelling. Apgar scores are 8 at 1 minute and 8 at 5 minutes. Within the first hour of birth, he has tachypnea, nasal flaring, and mild retractions. Chest auscultation reveals good air movement bilaterally; a few rales are noted.

- ▶ What is the most likely diagnosis?
- ▶ What is the best management for this condition?

### ANSWERS TO CASE 48: **Transient Tachypnea of the Newborn**

*Summary:* A term newborn born by cesarean section has respiratory distress.

- **Most likely diagnosis:** Transient tachypnea of the newborn (TTN).
- **Treatment:** Supportive care including supplemental oxygen, if necessary.

## ANALYSIS

### *Objectives*

1. Know the presentation of TTN.
2. Understand the medical care for TTN.

### *Considerations*

This infant presents soon after birth with mild respiratory distress following an uneventful pregnancy and delivery. Evaluation of this infant begins with auscultation of the lungs and heart.

APPROACH TO:

**Transient Tachypnea of the Newborn**

## DEFINITIONS

**TRANSIENT TACHYPNEA OF THE NEWBORN:** Slow absorption of fetal lung fluid with resultant tachypnea. The condition more commonly is associated with cesarean section deliveries.

**MECONIUM ASPIRATION SYNDROME:** Aspiration of meconium during delivery resulting in respiratory distress. Radiographic findings include hyperinflation with patchy infiltrates. As meconium may plug small airways, areas of air trapping are often present and may lead to the development of pneumothorax.

**RESPIRATORY DISTRESS SYNDROME:** A condition seen in premature infants resulting from surfactant deficiency. Radiographic findings include a characteristic reticulonodular “ground glass” pattern with air bronchograms and decreased aeration.

**CONGENITAL DIAPHRAGMATIC HERNIA (CDH):** The condition of herniation of abdominal contents through the posterolateral foramen of Bochdalek into the thoracic cavity. The incidence is approximately 1 in 5000 live births.

**EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO):** A system using a modified heart-lung machine utilized in severe pulmonary failure. Cannulation of the carotid artery and jugular vein is required to link the neonate to the system.

## CLINICAL APPROACH

Transient tachypnea of the newborn is a self-limited condition usually occurring in a **term infant** after an uneventful cesarean section (more commonly) or vaginal birth. It is felt to be caused by slow absorption of fetal

lung fluid. Infants with TTN develop respiratory distress shortly after birth with tachypnea, mild retractions, nasal flaring, and in more severe cases grunting and cyanosis. Chest radiography reveals **perihilar streaking and fluid in the fissures**; lungs are aerated. Most infants with TTN have resolution of their tachypnea in 24 to 96 hours.

For a few infants with TTN, oxygen saturations drop and supplemental oxygen is required; rarely does the oxygen requirement exceed 40%. In the rare, more severe case of TTN consideration for ongoing increased pulmonary vascular resistance leading to persistent pulmonary hypertension must be entertained. Infants with TTN do not require antimicrobial therapy; failure of the infant to follow the expected course of mild respiratory distress indicates the need to evaluate the child for more serious pathology.

Infants with **respiratory distress syndrome (RDS)** are usually born prematurely (less than 34 weeks gestational age); these infants have a deficiency of surfactant. Shortly after birth they present with symptoms of respiratory distress including poor oxygenation, grunting, retracting, and poor air movement. Radiographically they have findings including a reticulonodular pattern with air bronchograms and decreased aeration of the lungs. Supportive care includes supplemental oxygen as needed to maintain oxygen saturation of 90% to 95% and intravenous fluids or nasogastric feeding to maintain hydration as the degree of tachypnea usually precludes oral feeding. Exogenous surfactant is available and is administered by the resuscitation team in an effort to ameliorate the effects of surfactant deficiency.

## COMPREHENSION QUESTIONS

- 48.1 A term male is born to a 33-year-old woman who had little prenatal care. Immediately after birth he has cyanosis and respiratory distress. Chest auscultation in the delivery room reveals right-sided heart sounds and absent left-sided breath sounds. Which of the following is the most appropriate next step?
- A. Assess the abdomen to evaluate for possible congenital diaphragmatic hernia.
  - B. Order a computed tomography of the chest.
  - C. Order ultrasonography of the chest.



D. Perform a needle thoracostomy for possible pneumothorax.

E. Prepare the infant for ECMO.

48.2 A term female is born via repeat cesarean section to a 30-year-old woman. Immediately after birth she has mild respiratory distress. Chest auscultation in the delivery room reveals clear breath sounds. Which of the following is the most appropriate next step?

A. Endotracheal intubation with direct suction.

B. Begin intravenous antibiotic therapy.

C. Deliver surfactant therapy.

D. Observe and administer supplemental oxygen as needed.

E. Bag-and-mask ventilation.

48.3 A term male is born vaginally to a 22-year-old primigravida woman; the pregnancy was uncomplicated. Just prior to delivery, fetal bradycardia was noted, and at delivery thick meconium is found. The infant has hypotonia and brady-cardia. Which of the following is the first step in resuscitation?

A. Administration of epinephrine through endotracheal tube

B. Bag-and-mask ventilation

C. Endotracheal intubation with direct suction

D. Oxygen delivered by cannula in close proximity to the nares

E. Tracheostomy

48.4 After the infant discussed in Question 48.3 is stabilized and admitted to the neonatal intensive care unit, a chest radiograph reveals bilateral patchy infiltrates with coarse streaking and flattening of the diaphragm. He abruptly has an increased oxygen requirement. Physical examination reveals decreased right-sided breath sounds. Which of the following is an accurate statement?

A. High positive end-expiratory pressure (PEEP) is useful in this condition.

B. Needle thoracostomy is contraindicated.

C. Chest radiography is likely to reveal CDH.

- D. Chest radiography is likely to reveal a diffuse reticulonodular pattern.
- E. Transillumination of the chest is likely to transmit excessive light on the right side.

## ANSWERS

- 48.1 **A.** Evaluation of neonates born with respiratory distress and unilateral breath sounds includes an abdominal examination. With asymmetrical breath sounds, pneumothorax and CDH are considered. This infant's scaphoid abdomen suggests CDH; needle thoracostomy is avoided because intestinal perforation may occur. The patient is stabilized and the need for ECMO is ascertained after the infant's initial therapy response is evaluated. Many cases of CDH are diagnosed by prenatal ultrasound.
- 48.2 **D.** As this infant most likely has TTN the next step is to observe and administer supplemental oxygen as needed.
- 48.3 **C.** Endotracheal intubation with direct suction is performed in a **depressed** infant with thick meconium noted at delivery. Bag-and-mask ventilation or endotracheal intubation without suction may increase the volume of meconium aspirated. A vigorous infant with a heart rate greater than 100 beats per minute, strong respirations, and good muscle tone with meconium-stained need not be suctioned immediately after birth.
- 48.4 **E.** This infant likely has a right-sided pneumothorax; excessive light transmission by transillumination and right-sided hyperresonance with auscultation are expected. Infants with meconium aspiration and respiratory distress are at higher risk for pneumothorax, especially if high PEEP is used for oxygenation. A chest tube for the pneumothorax may be needed. Infants with severe respiratory distress or circulatory involvement may require emergent needle aspiration.
- 

## CLINICAL PEARLS

- Transient tachypnea of the newborn (TTN) is associated with birth by cesarean section.

- ▶ TTN is managed with supportive care and does not lead to chronic lung disease.
- 

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### CASE 49

A full-term 1-week-old boy presents with bilious vomiting and lethargy. His mother notes a normal prenatal course and uncomplicated delivery. On physical examination he is noted to have significant abdominal distension and blood in his diaper.

- ▶ What is the most likely diagnosis?
- ▶ What is the best management for this condition?

ANSWERS TO CASE 49: **Malrotation**

*Summary:* A full-term 1-week-old boy presents with bilious vomiting and lethargy. He is noted to have significant abdominal distension and blood in his diaper.

- **Most likely diagnosis:** Malrotation with volvulus.
- **Best treatment:** Surgical intervention to remove any necrotic bowel and to ensure adequate blood supply to surviving intestine.

## ANALYSIS

### *Objectives*

1. Know the presentation of malrotation with volvulus.
2. Understand the treatment of malrotation.
3. Be familiar with the differential diagnosis of acute abdominal pain in children.

### *Considerations*

In this neonate with bilious emesis, a variety of etiologies are possible ([Table 49-1](#)). The clues to the diagnosis are bilious emesis due to intestinal obstruction, abdominal distension, blood per rectum, and lethargy. The most important next step is surgical intervention to prevent death and loss of viable intestine.

Condition	Signs and Symptoms
Abdominal migraines	Recurrent abdominal pain with emesis
Appendicitis	Right lower quadrant pain, abdominal guarding, and rebound tenderness
Bacterial enterocolitis	Diarrhea (may be bloody), fever, vomiting
Cholecystitis	Right upper quadrant pain, which may extend subscapular
Diabetes mellitus	History of polydipsia, polyuria, and weight loss
Henoch-Schönlein purpura	Purpuric lesions, joint pain, blood in urine, and guaiac-positive stools
Hepatitis	Right upper quadrant pain and jaundice
Incarcerated hernia (inguinal)	Inguinal mass, lower abdominal or groin pain, emesis
Intussusception	Colicky abdominal pain and currant jelly stools

Malrotation (with volvulus)	Abdominal distention, bilious vomiting, blood per rectum, usually presents in infancy
Nephrolithiasis	Hematuria, colicky abdominal pain
Pancreatitis	(Severe) epigastric abdominal pain, fever, and persistent vomiting
Pneumonia (esp. left lower)	Fever, cough, rales on auscultation of the chest
Small-bowel obstruction	Emesis, frequent history of prior abdominal surgery
Streptococcal pharyngitis	Fever, sore throat, headache
Testicular torsion	Testicular pain and edema
Urinary tract infection	Fever, vomiting, and diarrhea in infants; back pain in older children

**Table 49-1 • COMMON ETIOLOGIES OF ACUTE ABDOMINAL PAIN IN INFANTS AND YOUNG CHILDREN**

APPROACH TO:

**Malrotation**

## DEFINITIONS

**VOLVULUS:** Twisting of the mesentery of the small intestine leading to decreased vascular perfusion, which results in ischemia and ultimately bowel

necrosis.

**INTUSSUSCEPTION:** A condition in which a proximal portion of the gastrointestinal tract telescopes into an adjacent distal portion. The most common location is ileocolic portion of the bowel.

## CLINICAL APPROACH

**Malrotation occurs when intestinal rotation is incomplete during fetal development.** During normal fetal development in the first trimester, the growing intestine exits the abdominal cavity, elongates, and ultimately rotates 270° in a counterclockwise manner before returning into the abdomen. Following normal intestinal rotation, the duodenojejunal junction (ligament of Treitz) is fixed to the posterior body wall to the left of the spine. In cases of malrotation, the ligament of Treitz is located on the right side and the intestine may use the small portion of attached mesentery as axis to turn (volvulus) leading to ischemia and possible necrosis.

Although individuals with intestinal malrotation may present from birth to adulthood, the classic presentation is that of an infant with bilious vomiting due to intestinal obstruction. With prolonged ischemia the bowel becomes necrotic and the patient may have melena or hematemesis, and may develop peritonitis, acidosis, and sepsis. Without surgical intervention, risk of mortality is significant. Patients with malrotation and either partial or intermittent volvulus may present with recurrent abdominal pain or lymphatic congestion leading to failure to thrive because of malabsorption or chylous ascites. Individuals may also have asymptomatic malrotation as an incidental finding.

Abdominal radiographs may be normal or have nonspecific findings in cases of volvulus; thus an upper gastrointestinal contrast series is generally indicated. The characteristic finding in cases of volvulus is a “corkscrew” pattern of the duodenum or “bird’s beak” of the second or third portions of the duodenum. In cases of malrotation with or without volvulus, abnormal position (right sided) of the ligament of Treitz or malposition of the colon may be noted with contrast radiography.

Prior to **emergent** surgical intervention, the initial management of patients with malrotation and volvulus includes appropriate evaluation of fluid status as patients may have significant fluid loss with electrolyte abnormalities. In

the ill-appearing infant, placement of a nasogastric tube to aid gastrointestinal decompression, and initiation of parenteral antibiotic, in order to address potential sepsis are indicated. Exploratory laparotomy is performed and bowel viability assessed. Areas of necrotic bowel are removed and Ladd procedure of disengaging bowel with anomalous fixation and appendectomy are performed. Complications include short gut syndrome if a significant portion of necrotic bowel is removed, and adhesions may develop leading to obstruction. Because of the significant mortality and morbidity associated with volvulus, asymptomatic patients with malrotation require surgical intervention.

## COMPREHENSION QUESTIONS

- 49.1 Malrotation with volvulus is most likely to be present in which of the following patients?
- A. A healthy 15-month-old with severe paroxysmal abdominal pain and vomiting
  - B. A 15-year-old sexually active girl with lower abdominal pain
  - C. A 3-day-old term infant with bilious emesis, lethargy, and abdominal distension
  - D. A 4-day-old premature baby (33-week gestation) who has recently started nasogastric feeds; he now has abdominal distention, bloody stools, and thrombocytopenia
  - E. A 7-year-old non-toxic-appearing girl with abdominal pain, vomiting, fever, and diarrhea
- 49.2 A 3-day-old boy presents with 12 hours of bilious vomiting, abdominal pain, and abdominal distension. Which of the following is the most appropriate next step in management?
- A. Order an abdominal ultrasonography.
  - B. Order a computed tomography scan of the abdomen.
  - C. Order an upper GI contrast series.
  - D. Order a barium enema.
  - E. Order a chest radiograph.



- 49.3 A 9-year-old boy has 24 hours of persistent abdominal pain and vomiting. His physical examination reveals abdominal guarding and right lower quadrant rebound tenderness. Which of the following is the most likely diagnosis?
- A. Appendicitis
  - B. Gastroenteritis
  - C. Gastroesophageal reflux
  - D. Intussusception
  - E. Pyloric stenosis
- 49.4 A previously healthy 18-month-old child has vomiting and severe, paroxysmal, writhing abdominal pain (he prefers to have his knees flexed to the chest) alternating with periods of relative comfort with a soft, only mildly tender abdomen. On abdominal examination you find a sausage-like mass. He has not stoolled, but you find blood upon digital rectal examination. Which of the following is the best next step in management?
- A. Administer morphine for pain control.
  - B. Order a computed tomography of the abdomen.
  - C. Obtain an air contrast enema.
  - D. Obtain serum acetaminophen levels.
  - E. Begin antibiotics for *Escherichia coli* 0157:H7.
- 49.5 A 6-week-old male infant has projectile emesis after feeding. He has an olive-shaped abdominal mass on abdominal examination. Which of the following statements is accurate?
- A. He likely has hypochloremic metabolic alkalosis.
  - B. He likely has metabolic acidosis.
  - C. This condition is more common in female infants.
  - D. He should be restarted on feeds when the vomiting resolves.
  - E. He likely will develop diarrhea.

## ANSWERS

- 49.1 C. The 3-day-old term infant with bilious emesis and abdominal distension has classic presenting features of malrotation with volvulus. The 15-month-old child with paroxysmal abdominal pain is most likely to have intussusception. The adolescent female is evaluated for ectopic pregnancy, pelvic inflammatory disease, appendicitis, ovarian torsion, and ruptured ovarian cyst. The premature infant might have necrotizing enterocolitis, whereas the 7-year-old girl most likely has gastroenteritis.
- 49.2 C. Order an upper GI contrast series. Fluid and electrolyte status should also be evaluated.
- 49.3 A. This child most likely has appendicitis based on the clinical presentation.
- 49.4 C. The case describes the typical presentation of intussusception. Although a clinical diagnosis can be made, the diagnostic “gold” standard and often treatment is contrast enema. Air contrast usually is preferred because the complication risk is lower than with other forms of contrast material. Prior to diagnostic intervention, patients should undergo measurement of serum electrolyte and hemoglobin levels and receive fluid resuscitation. When suspicion for intussusception is high, a pediatric surgeon should be consulted. Classically described “currant jelly stools” are a late finding. Recurrence of intussusception following successful reduction occurs in 5% to 10% of cases.
- 49.5 A. This infant has the features of pyloric stenosis, a condition four times more common in males and more common in first-born children. Affected infants usually present between the third and eighth week of life with increasing projectile emesis. Abdominal examination may reveal an olive-shaped mass and visible peristaltic waves. Serum electrolyte levels usually reveal hypochloremic metabolic alkalosis. Ultrasonography is useful in confirming the diagnosis.
- 

## CLINICAL PEARLS

- Treatment of malrotation with volvulus includes emergent surgical intervention.
- Classic features of intussusception are fever, intermittent colicky abdominal pain, currant jelly stools, and a sausage-like abdominal mass.

- Classic features of pyloric stenosis include projectile vomiting, an olive-shaped abdominal mass, and **hypochloremic metabolic alkalosis**.
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### CASE 50

A 13-year-old girl complains about “zits” on her face and shoulders. She has tried over-the-counter benzoyl peroxide to no avail, and has stopped eating

chocolate and french fries on her mother's advice. She has been invited to an upcoming school dance and wants to look her best. She complains about blackheads, but also lesions that are deep and painful.

- ▶ What is the diagnosis?
- ▶ What is the best treatment for her condition?

## ANSWERS TO CASE 50: **Acne Vulgaris**

*Summary:* An adolescent girl presents with acne on her face and shoulders.

- **Most likely diagnosis:** Combination acne.
- **Best therapy:** First-line therapy includes antibacterial soap, keratolytic agent (benzoyl peroxide), comedolytic agent (tretinoin), and/or topical antibiotic (erythromycin). Oral antibiotics (tetracycline) are a secondary option. Isotretinoin (oral tretinoin) is reserved for severe, resistant nodulocystic acne.

## ANALYSIS

### *Objectives*

1. Understand the various types of acne vulgaris.
2. Know the treatments for various types of acne.
3. Discuss the potential side effects of isotretinoin.

### *Considerations*

Acne vulgaris has the potential to be as damaging to the psyche as it can be to the skin. Managing acne successfully involves promoting patient understanding of the basics behind its development, creating thoughtful treatment regimens tailored to each patient, and periodically reassessing acne control in an effort to prevent possible emotional and physical scarring.

### APPROACH TO:

#### **Acne Vulgaris**

## DEFINITIONS

**COMEDONE:** Open comedones (blackheads) are composed of compacted melanocytes; closed comedones (whiteheads) contain purulent debris.

**CYST:** Dilated and often tender intradermal follicle.

**PAPULE:** Small, erythematous, and inflamed “bump” under the skin due to sebum, fatty acids, and bacteria reacting within a follicle.

**NODULE:** Papule greater than 5 mm penetrating deep into the dermis.

**PUSTULE:** Elevated focus of inflammation and purulent exudate around a comedone, occurring in the superficial dermis.

## CLINICAL APPROACH

**Pubertal hormonal surges lead to an increase in sebum production by sebaceous glands.** Proliferation of the bacterium *Propionibacterium acnes* leads to distention of follicular walls, causing obstruction of sebum flow. Follicles reach a maximum capacity and rupture, releasing their inflammatory contents. Neutrophils and liposomal enzymes are released, causing further inflammation. Scarring and pitting often may result.

Acne lesions are categorized as inflammatory or noninflammatory. Noninflammatory lesions consist of open and closed comedones. Inflammatory lesions are characterized by the presence of papules, pustules, nodules, or cysts.

Treatment goals are elimination of lesions and diminishment of scarring ([Table 50-1](#)). Improvement may not be noticed for at least a month after therapy is initiated, with flare-ups possible during treatment. Patients should be discouraged from manipulating skin lesions because doing so will increase inflammation and promote scarring. The affected skin should be gently washed using antibacterial soap and rinsed well to prevent soap buildup on the skin surface. Scrubbing agents and harsh soaps should not be used, since they may stimulate more oil production and promote acne.

Acne Type	Treatment <sup>a</sup>
Pure comedonal acne	Topical tretinoin or adapalene at night
Mild papular acne	Benzoyl peroxide in the morning and at night
Papulopustular and cystic (inflammatory) acne	Benzoyl peroxide and/or topical antibiotics in the morning, and topical tretinoin or adapalene at night
Severe pustulocystic acne	Benzoyl peroxide and oral antibiotic
Severe cystic acne	Oral retinoid (isotretinoin)

<sup>a</sup>Wash all types with antibacterial soap in the morning and at night.

**Table 50-1 • TREATMENT OF VARIOUS TYPES OF ACNE**

**First-line management should begin with topical benzoyl peroxide or a comedolytic agent such as a retinoid (Retin-A).** The combination of benzoyl peroxide in the morning and a comedolytic agent at night may be effective when either alone has failed. Benzoyl peroxide must be washed off prior to application of tretinoin or the retinoid will be rendered ineffective. Benzoyl peroxide is bactericidal and keratolytic, causing follicular desquamation. It is available in over-the-counter preparations with variable uniformity, stability, and efficacy. Although these over-the-counter preparations eliminate bacteria at the skin surface, they do not have a carrier vehicle that allows deep follicular penetration. Therefore, 2.5% to 10% prescription preparations are preferable, with gels being more efficacious although more irritating at times; starting at the lowest concentration is recommended. A benzoyl peroxide wash is beneficial when lesions are widely distributed or when adherence to a treatment plan is problematic. Washes are applied in the shower and then rinsed off after approximately 30 seconds. Benzoyl peroxide can bleach fabric, so careful and thorough drying is recommended.

**Topical tretinoin, a vitamin A derivative, inhibits the formation of micro-comedones and increases cell turnover.** Therapy should begin conservatively at 0.025%, with 3 to 4 weeks allowed for accommodation. Patients should use a mild soap (Dove or Cetaphil) and allow the skin to dry 20 to 30 minutes prior to applying nightly tretinoin. Mild redness and peeling can occur, and patients should avoid sun exposure and use sunscreens. Adapalene 0.1% (Differin) is a retinoid formulation that causes less irritation and photosensitivity, has more activity, and can be used concomitantly with benzoyl peroxide preparations. A combination product combining adapalene and benzoyl peroxide (Epiduo Gel 0.1%/2.5%) is available. Tazarotene 0.1% (Tazorac) is a retinoid that is active against psoriasis. This agent is teratogenic and causes irritation, so it should be used with caution. Some believe that azelaic acid applied twice daily for 4 to 6 months may provide acne relief, especially for those sensitive to other agents, and theoretically can reduce scarring.

**Topical, rather than systemic, antibiotics are preferred because of their fewer side effects.** Topical antibiotics (erythromycin, clindamycin) often are applied to affected areas twice daily or in combination with benzoyl peroxide or tretinoin. Long-term topical or oral antibiotic monotherapy is not recommended due to the potential development of bacterial resistance. Combination benzoyl peroxide and topical antibiotic preparations can be particularly beneficial, and do not typically promote resistance. Oral antibiotics are used when moderate to severe inflammatory and pustular acne does not respond to topical treatment. Tetracycline is the most frequently used oral antibiotic because it is inexpensive and has few side effects. To minimize the potential for antibiotic resistance, oral antibiotics ideally should be discontinued after a few months. Antibiotics, irrespective of the formulation, should be discontinued once inflammatory lesions are under good control.

**Isotretinoin is the treatment of choice for severe, resistant nodulocystic acne.** A 5-month course often clears a severe case of acne. It is highly teratogenic and has many side effects, including **cheilitis, conjunctivitis, hyperlipidemia, blood dyscrasias, elevated liver enzymes, and photosensitivity.** Lipid levels, liver enzymes, and complete blood counts should be monitored monthly during the course. Females should have a negative pregnancy test immediately before isotretinoin is initiated and should maintain effective contraception before, during, and after therapy. Prescribers



and patients must be registered in the iPLEDGE<sup>TM</sup> pregnancy prevention and risk management program.

Oral contraceptives (Ortho Tri-Cyclen) are approved for treatment of acne, and intralesional steroid therapy is sometimes used in unresponsive cases.

## COMPREHENSION QUESTIONS

- 50.1** A teenager with severe cystic acne started using isotretinoin a month ago. Initially her acne worsened, but is now starting to improve. However, she reports “not feeling normal.” She does not want to go to school, cries frequently, and feels hopeless, but declares no suicidal thoughts. She also feels “achy” all over. Which of the following is the best course of action?
- A. Continue isotretinoin and see her in follow-up in a week.
  - B. Prescribe an antidepressant.
  - C. Discontinue isotretinoin and refer her to a psychiatrist.
  - D. Decrease her isotretinoin dose to determine if the side effects resolve.
  - E. Counsel her that these symptoms will resolve over time.
- 50.2** A teenage boy complains of a several-week history of facial “zits” that are painful and itchy. There are no other breakouts. He has inflammatory papules and pustules in the beard and moustache area and has mild cervical lymphadenopathy. He occasionally works weekends on a farm. Which of the following therapies is appropriate?
- A. Topical isotretinoin
  - B. Topical hydrocortisone
  - C. Oral antifungal
  - D. Topical mupirocin
  - E. Oral acyclovir
- 50.3** A 7-day-old infant is brought to clinic because of “pimples” on his cheeks and forehead. He is breast-feeding well, and the parents have no other concerns. The skin around the pimples and elsewhere is



unremarkable, as is the rest of his examination. Which of the following is appropriate advice or therapy?

- A. Recommend a different soap.
- B. Prescribe topical triamcinolone.
- C. Prescribe topical erythromycin.
- D. Recommend no treatment.
- E. Recommend more frequent bathing.

**50.4** A 17-year-old girl is prescribed oral tetracycline, topical tretinoin, and topical benzoyl peroxide. She is sexually active and takes an oral contraceptive. You should counsel her to do which of the following?

- A. Take the tetracycline with food or milk.
- B. Use a second form of birth control in addition to her oral contraceptive.
- C. Get some sun to help dry up her acne.
- D. Avoid chocolate and fried foods.
- E. Avoid sunscreen because it will irritate her face.

## ANSWERS

**50.1** C. Depression is a rare side effect of isotretinoin, but it can be severe and suicides have been reported. Myalgias and arthralgias have also occurred. It would be best to stop the drug and have the patient evaluated for depression.

**50.2** C. Tinea barbae is caused by various dermatophytes and closely resembles tinea capitis. It can be acquired through animal exposure and is more common in farmers. Topical antifungal preparations are ineffective; oral antifungals are required.

**50.3** D. Approximately 20% of normal neonates develop at least a few comedones within the first month of life. The cause of neonatal acne is unknown, but has been attributed to placental transfer of maternal androgens, hyperactive adrenal glands, and a hypersensitive neonatal end-organ response to androgenic hormones. Such patients may be

predisposed to adolescent acne. In most cases a prescription or change in skin care is not warranted.

**50.4 B.** Oral antibiotics may decrease the effectiveness of oral contraceptive pills. Tretinoin can lead to photosensitivity; patients should avoid sun exposure or use sunscreen. Diet has not been found to have an effect on acne. Tetracycline should be taken on an empty stomach; milk products bind tetracycline.

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### CLINICAL PEARLS

- Acne is a disorder of the sebaceous follicle in which excess sebum, keratinous debris, and bacteria accumulate, producing microcomedones that may become inflamed.
  - Treatment of acne depends on its severity and distribution, and may involve a regimen of oral or topical agents, alone or in combination.
- 

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## CASE 51

A 3700-g male infant is born at 38 weeks' gestation after a pregnancy with limited prenatal care. The infant is noted after birth to have a dribbling urinary stream and a lower abdominal mass. Postnatal ultrasonography reveals bilateral hydronephrosis with bladder wall hypertrophy and an enlarged urethra.

- ▶ What is the most likely diagnosis?
- ▶ What is the most appropriate next test?

### ANSWERS TO CASE 51: **Posterior Urethral Valves**

*Summary:* A term newborn male has evidence of severe urinary obstruction.

- **Most likely diagnosis:** Posterior urethral valves (PUV).
- **Most appropriate next test:** Renal ultrasonography (USG).

## ANALYSIS

### *Objectives*

1. Know the various presentations of patients with PUV.
2. Know the possible long-term sequelae associated with PUV.
3. Be familiar with common abdominal masses in the newborn period.

## ***Considerations***

Many conditions cause abdominal masses in the newborn ([Table 51-1](#)). In this infant's case, the dribbling urinary stream suggests PUV. An abdominal USG is a useful and noninvasive tool to aid in the diagnosis.

### **Hepatic enlargement**

- Cardiac failure, arrhythmias
- Hepatic tumors (mesenchymal hamartoma, hemangioma, hemangioendothelioma, metastatic tumors such as neuroblastoma)
- Metabolic disorders (storage diseases [lysosomal or carbohydrate], tyrosinemia, galactosemia)
- Beckwith-Wiedemann syndrome
- Congenital infections (cytomegalic inclusion disease, syphilis, toxoplasmosis, rubella)

### **Pelvic masses**

- Ovarian cyst (follicular, dermoid, teratoma)
- Hydrocolpos, hydrometrocolpos
- Imperforate hymen
- Vaginal atresia/stenosis
- Cloaca

### **Adrenal masses**

- Adrenal hemorrhage
- Neuroblastoma

### **Renal mass**

- Multicystic or polycystic kidney
- Hydronephrosis (posterior urethral valves, ureterovesical or ureteropelvic junction obstruction)
- Renal vein thrombosis

### **Retroperitoneal masses**

- Neuroblastoma
- Wilms tumor
- Mesoblastic nephroma
- Sacrococcygeal teratoma
- Lymphangioma

### **Gastrointestinal masses**

- Duplication
- Mesenteric cyst

*Data from Seashore JH. Distended abdomen. In: McMillan JA, DeAngelis CD, Feigin RD, Warshaw JB, eds. Oski's Pediatrics. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 1999:323.*

## Table 51-1 • ABDOMINAL MASSES CAUSING DISTENTION

APPROACH TO:

**Posterior Urethral Valves**

### DEFINITIONS

**VESICoureTERAL REFLUX (VUR):** Retrograde urine flow from the bladder into the ureter(s) and, if severe, into the kidney. In general this condition is more common in females and may lead to recurrent urinary tract infections (UTI) and diminished renal function. Depending on the degree of reflux, treatment ranges from antibiotic prophylaxis to surgical intervention.

**VOIDING CYSToureTHROGRAM (VCUG):** A radiographic study in which a catheter is placed in the bladder and contrast is instilled. Upon voiding, the urethra is visualized and, in cases of vesicoureteral reflux, the ureters are outlined.

### CLINICAL APPROACH

**Fetal ultrasonography** assists in the prenatal diagnosis of urinary tract obstruction. Sonographic findings include **bilateral hydronephrosis with bladder distention with a “keyhole” appearance**, particularly in a male fetus. In severe cases oligohydramnios is found and may lead to poor fetal lung development with pulmonary insufficiency and congenital contractures. Prenatal ultrasonography leads to the diagnosis in most cases of PUV.

Urethral valves are leaflets of tissue located in the lumen of the distal urethra from the prostate to the external sphincter. **Posterior urethral valves are the most common cause of severe urinary tract obstruction in boys**, occurring in 1 of every 5000-8000 newborn males; 25% to 30% ultimately have end-stage renal disease or chronic renal insufficiency. Neonates present with distended bladders, poor or dribbling urinary streams, palpable kidneys, reduced renal function, or UTI. Older infants have failure to thrive, renal dysfunction, or UTI. Older boys may present with voiding difficulty, such as diurnal enuresis or frequency. Posterior urethral valve is confirmed with VCUG or postnatal USG. The evaluation of the boy who has UTI includes VCUG and renal USG.

Immediate relief of PUV obstruction includes bladder catheterization through the urethra with a small feeding tube. If UTI is suspected, antimicrobial therapy is initiated. Serum electrolytes, blood urea nitrogen, and creatinine levels are measured with correction as needed. Hemodynamic status is monitored because sepsis or renal failure can lead to cardiovascular collapse.

After acute obstruction is relieved and the patient has been stabilized, endoscopic transurethral valve ablation may be performed if the serum creatinine level is normal and urethral size permits. If the serum creatinine remains elevated, the urethral lumen is too narrow, or the UTI does not respond to antibiotics, emergent vesicostomy may be necessary. Following ablation, VUR and persistent hydroureteronephrosis may occur.

### ***Follow-Up***

After surgery, patients require surveillance of renal function and for possible UTI. Many patients will have polyuria because of diminished ability to concentrate the urine and are at greater risk for dehydration.

Routine care for boys with a history of PUV includes regular monitoring with urinalysis, renal USG, serum electrolyte levels, blood pressure, and linear growth. They may have prolonged diurnal enuresis and may require urodynamic studies to evaluate their voiding. Renal insufficiency is common, and some may require renal transplantation.

## **COMPREHENSION QUESTIONS**

- 51.1 A 3-month-old boy presents with fever without a source. As part of his evaluation a urinalysis is performed; a UTI is suspected. Which of the following is the best next step?
- A. If the urine culture reveals UTI, renal USG and VCUG should be performed.
  - B. VCUG should be performed only after a second UTI is diagnosed.
  - C. Antibiotics should be initiated after urine culture and sensitivities are obtained.
  - D. Renal biopsy should be performed.

E. Preferred methods of collection for urine culture for this infant include midstream clean-catch and bag urine.

51.2 A 1-month-old girl presents with fever and vomiting. Her serum white blood cell (WBC) count is elevated. Urinalysis reveals 100 WBC per high-power field (unspun); it is positive for nitrates and leukocyte esterase. Urine culture results confirm a UTI; renal USG and VCUG show mild to moderate hydronephrosis and grade III VUR on the right. Which of the following is the best next step?

- A. She will require surgical reimplantation of her right ureter.
- B. Antimicrobial prophylactic therapy should be started when her current course of antibiotics is completed.
- C. VCUG should be performed on a monthly basis.
- D. Subsequent urine specimen must be obtained only by suprapubic aspiration.
- E. Renal arteriography is indicated.

51.3 A 6-month-old infant male presents to your clinic with an abdominal mass, which was discovered by his new foster mother during the child's bath. On physical examination, you also find macroglossia and right-sided hemihyper-trophy. This infant is likely to have which of the following?

- A. Down syndrome with duodenal atresia
- B. Alagille syndrome and biliary atresia
- C. Beckwith-Wiedemann syndrome with Wilms tumor
- D. Neurofibromatosis and abdominal neurofibromas
- E. Zellweger syndrome and hepatomegaly

51.4 An 8-year-old boy presents with bedwetting 3 to 4 times per week for "as long as he can remember." He has a strong urine stream, daytime urine continence, and no UTIs. His physical examination is normal. Which of the following is the most appropriate next course of action?

- A. Urodynamic studies.
- B. Reassurance; he has secondary nocturnal enuresis.
- C. Use of enuresis alarm.



- D. Desmopressin acetate can be administered every 6 hours to control enuresis.
- E. Behavior modification that includes punishment for wet nights and rewards for dry nights.

## ANSWERS

- 51.1 A. For any male infant with a UTI, evaluation of anatomy and function is necessary. The preferred methods of urine collection include bladder catheterization and suprapubic bladder aspiration. Antimicrobial therapy is started empirically while awaiting urine culture and sensitivity results.
- 51.2 B. Infants and children with VUR as described typically receive prophylactic antimicrobial therapy (although the benefit of this therapy on lower grade disease has been questioned) and close monitoring for infection with urinalysis and urine culture at 3- to 4-month intervals. Sulfamethoxazole-trimethoprim, trimethoprim alone, and nitrofurantoin are commonly used for antimicrobial prophylaxis, VUR is graded from I to V based on the degree of reflux. Higher-grade reflux is less likely to resolve spontaneously and is more likely to result in renal damage.
- 51.3 C. This infant with features of Beckwith-Wiedemann syndrome is at high risk for developing Wilms tumor, hepatoblastoma, and gonadoblastoma.
- 51.4 C. Nocturnal enuresis occurs in 15% of 5-year-olds with a resolution rate of 15% per year. Males are more frequently affected, and family history is common. Initial evaluation includes a history of wetting pattern, prior UTI, and developmental, social, and emotional history. Physical examination includes kidney palpation, neurologic examination, and examination of the back looking for sacral dimple or hairy nevus. Some recommend urinalysis and culture to rule out occult infection. The enuresis alarm has a success rate of 70% to 90% and requires parental support. Pharmacologic interventions include nighttime doses of imipramine or oral desmopressin acetate. Intranasal formulations of desmopressin are no longer approved for the treatment of primary nocturnal enuresis. Following use of desmopressin acetate, fluid intake is restricted to avoid hyponatremia. Pharmacologic treatment usually is reserved for special occasions, such as when the child is sleeping over at

a friend's house, summer camp, and so on. Behavior modification does not include punishment.

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## CLINICAL PEARLS

- ▶ Posterior urethral valve occurs exclusively in males.
  - ▶ Boys with posterior urethral valve are at risk for end-stage renal disease, even after appropriate therapy.
- 

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## CASE 52

The mother of a healthy 8-year-old boy is concerned about his school performance. At the last parent–teacher conference, his teacher noted that he is easily distracted and routinely fails to complete both homework assignments and classroom papers. His mother states that at home he also has difficulty in completing tasks and he fidgets constantly. Although the child is very talkative, he does not answer questions clearly. His physical examination is significant only for fidgeting.

- ▶ What is the most likely diagnosis?
- ▶ What is the next step in management?

### ANSWERS TO CASE 52: Attention-Deficit/Hyperactivity Disorder

*Summary:* An 8-year-old easily distractible, hyperkinetic boy who cannot complete school work or stay on task at home.

- **Most likely diagnosis:** Attention-deficit/hyperactivity disorder (ADHD).
- **Next step in management:** An ADHD evaluation, which includes information regarding his behavior obtained from both the caregiver and the classroom teacher.

## ANALYSIS

### *Objectives*

1. Understand the basic evaluation of the child with symptoms of ADHD.
2. Know the various treatment options available for this condition.

### ***Considerations***

This boy exhibits ADHD behaviors, including easy distractibility, inability to focus and complete tasks, and excessive fidgeting. The next step is a complete ADHD evaluation as described. If data suggest ADHD, he should undergo developmental and psychological evaluations for coexisting psychiatric conditions or learning disability. Target outcomes then can be identified and a behavioral therapy, classroom modification, and possibly medication treatment plan designed.

APPROACH TO:

**Attention-Deficit/Hyperactivity Disorder**

## **DEFINITION**

**ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD):** A condition consisting of developmentally inappropriate inattentiveness, hyperactivity, and impulsivity.

## **CLINICAL APPROACH**

The *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV) describes **criteria** of **inattentiveness** and **hyperactivity/impulsivity** necessary to make an **ADHD diagnosis**. Attention-deficit/hyperactivity disorder is estimated to affect 3% to 10% of school-aged children with a significant male predominance; 25% of ADHD patients have an affected primary relative. The pathophysiology of ADHD remains to be elucidated, but decreased activity of certain brain regions in the frontal lobes may be responsible.

**Inattention criteria of ADHD** include careless mistakes, having difficulty paying attention, not listening, not completing assigned tasks, avoiding sustained mental effort, frequently losing things, easy distractibility, and forgetfulness.

**Hyperactivity criteria of ADHD include** frequent fidgeting, being out of his or her seat frequently, running or climbing excessively, having difficulty playing quietly, and often talking excessively.

**Impulsivity criteria of ADHD include** blurting out answers, having difficulty waiting for his or her turn, and interrupting or intruding frequently.

Attention-deficit/hyperactivity disorder is subdivided into three types: ADHD/I (at least 6 of 9 inattention behaviors), ADHD/HI (at least 6 of 9 hyperactive/impulsive behaviors), and ADHD/C (at least 6 of 9 of both the inattention and hyperactive/impulsive behaviors). Symptoms must be present for **at least 6 months in two or more settings, some symptoms must have been present before the age of 7, and symptoms must result in impaired function.** Caregivers and classroom teacher(s) provide the critical information by filling out checklists, such as the Conners rating, the ADHD index, the Swanson, Nolan, and Pelham checklist (SNAP), or the ADD-H comprehensive teacher rating scale (ACTeRS). Alternatively, information can be surmised through narratives or descriptive interviews.

**Psychological and developmental testing is part of the evaluation of an ADHD child; coexisting psychological and learning disorders occur frequently.** Common coexisting conditions include oppositional-defiant disorder (35.2%), conduct disorder (25.7%), anxiety disorder (25.8%), and depressive disorder (18.2%). Approximately 12% to 60% of ADHD children have concurrent learning disorders and may benefit from special education services.

Management includes the implementation of a long-term treatment program in collaboration with caregivers and teachers. The care plan includes setting specific goals such as increasing independence, decreasing disruptive behavior, improving academic performance, organization, and task completion, and improving relationships with family members, teachers, and peers. **Behavioral modification** can be used alone or in conjunction with **pharmacologic therapy.** Positive reinforcement (providing rewards or privileges) and negative consequences (time-out or withdrawal of privileges) emphasize appropriate behavior. Small class size, structured work, stimulating schoolwork, and appropriate seating arrangements can help **decrease disruptive classroom behaviors. Medications are often used to assist in treatment. Stimulant medications are considered first-line pharmacologic therapy to decrease ADHD behaviors.** Commonly used

stimulant medications include **methylphenidate and dextroamphetamine**. **Atomoxetine (Strattera)** is a **nonstimulant, selective norepinephrine reuptake inhibitor** approved for use in adults and children. Tricyclic antidepressants, clonidine and bupropion, often prescribed under the direction of a psychiatrist or neurologist, are also used.

Long-term sequelae of ADHD include poor peer relationships, poor fine motor control, and increased risk of accidents. Adolescents may develop substance abuse problems as a comorbid condition, but this comorbidity does not seem to be related to treatment of ADHD with stimulants. Approximately 50% of children function well in adulthood; others demonstrate continued inattention and impulsivity symptoms.

## COMPREHENSION QUESTIONS

- 52.1 An 8-year-old boy presents because his mother is concerned that he has ADHD. At home he is always restless, never seems to pay attention, and is always losing things. In the clinic, the child is cooperative and has a normal examination. Which of the following is the best next step in management?
- A. Give the child a 2-week trial of stimulant medication.
  - B. Obtain further information from the parents and teachers.
  - C. Reassure the child's mother that this behavior is age appropriate.
  - D. Send the child for psychological assessment.
  - E. Send the child for psychiatric evaluation.
- 52.2 A 7-year-old boy appears distracted. His mother notes that he daydreams "all of the time," and when he is daydreaming he does not respond to her. She describes the episodes as short (lasting several seconds) and occurring many times per day. When he is not daydreaming, he is attentive and can complete tasks. His behavior in class is not disruptive. Which of the following is the best next step in management?
- A. Obtain further information from his parents and teachers with the Conners rating scale.
  - B. Begin a program of behavioral modification.
  - C. Reassure the child's mother that this behavior is age appropriate.

- D. Send the child for an electroencephalogram.
  - E. Send the child for psychological assessment.
- 52.3 A 14-year-old adolescent male was recently diagnosed with ADHD. His evaluation for coexisting psychiatric disorders is most likely to identify which of the following?
- A. Bipolar disorder
  - B. Oppositional-defiant disorder
  - C. Pervasive developmental disorder
  - D. Posttraumatic stress disorder
  - E. Schizophrenia
- 52.4 An 8-year-old boy has completed the initial ADHD evaluation, which demonstrates that he meets 7 of the 9 criteria for inattention and that he also has many impulsive behaviors. Which of the following is the most appropriate next step in management?
- A. Give the child a 2-week trial of stimulant medication.
  - B. Arrange for special education placement.
  - C. Send the child for a complete psychoeducational assessment.
  - D. Send the child for an electroencephalogram.
  - E. Reassure the child's mother that this behavior is age appropriate.

## ANSWERS

- 52.1 **B.** A physical examination (with emphasis on the neurologic component) is completed to identify any soft signs of neurologic conditions. If none are found, he should undergo an ADHD evaluation with ADHD-specific behavior information obtained from caregivers and teachers. A diagnosis is considered if he has ADHD-specific behaviors in two or more settings. His ability to maintain focus during a brief visit to your clinic does not preclude the diagnosis of ADHD.
- 52.2 **D.** This child does not fit the classic ADHD pattern. Episodes of “daydreaming,” which last several seconds, may be petit mal or absence seizures; an electroencephalogram is needed.

- 52.3 B. Common coexisting psychiatric conditions include oppositional-defiant disorder (35.2%), conduct disorder (25.7%), anxiety disorder (25.8%), and depressive disorder (18.2%).
- 52.4 C. Prior to developing a management plan, the child is assessed for coexisting psychiatric and learning disorders (psychoeducational testing). Management can include stimulant medication, behavioral modification, and therapy appropriate for coexisting conditions.
- 

### CLINICAL PEARLS

- Attention-deficit/hyperactivity disorder (ADHD) is considered in children who have specific behaviors in two or more settings, such as at home and school or work.
  - Children with ADHD frequently have coexisting psychiatric or learning disorders, including oppositional-defiant disorder, conduct disorder, anxiety disorder, and depression.
  - Commonly used pharmacologic agents for treatment of ADHD are methylphenidate and dextroamphetamine.
- 

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## CASE 53

A previously healthy 12-year-old boy has had right knee pain for 3 weeks. He is athletic, playing basketball and running track, but he denies recent trauma. He describes increased pain when he is running or jumping. He has a normal physical examination except for mild edema and tenderness over his right tibial tubercle.

- ▶ What is the most likely diagnosis?
- ▶ What is the next step in management?

### ANSWERS TO CASE 53: Osgood-Schlatter Disease

*Summary:* A 12-year-old boy presents with knee pain that increases with activity and tenderness and swelling of his tibial tubercle of the affected knee.

- **Most likely diagnosis:** Osgood-Schlatter disease.
- **Next step in management:** For most patients rest and ice after activity; in severe cases, knee immobilization.

## ANALYSIS

### *Objectives*

1. Know the presentation and treatment of Osgood-Schlatter disease (OSD).
2. Know differential diagnosis of childhood bone pain and extremity swelling.

### *Considerations*

A history is critical to determine whether other signs and symptoms are present in this adolescent who has knee pain and swelling. His lack of constitutional signs and symptoms (fever, joint erythema, fatigue, weight loss, night sweats, bruising, and cough) are clues to the relatively benign nature of this condition. If any of these signs or symptoms is present, evaluation for more serious, potentially life-threatening conditions, such as malignancy, is appropriate.

APPROACH TO:

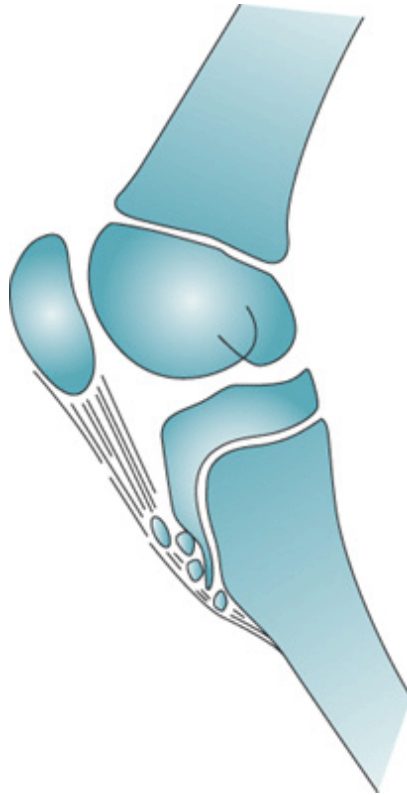
**Osgood-Schlatter Disease**

## DEFINITION

**OSGOOD-SCHLATTER DISEASE (OSD):** A condition of painful inflammation of the tibial tubercle.

## CLINICAL APPROACH

The **knee pain of OSD** is caused by **inflammation of the tibial tubercle, an extension of the tibial epiphysis or growth plate**. Ossification centers begin to form in children between the ages of 9 and 13 years and are completed between the ages of 15 and 17 years. Patients with OSD usually are males who present in late childhood through early adolescence. **Repetitive running and jumping** motions cause traction and microstress fractures to the developing area, resulting in inflammation, edema, tenderness, and bony changes (see [Figure 53-1](#)).



**Figure 53-1.** Osgood-Schlatter disease with the prominence of the tibial tuberosity in addition to ossicles separate from the anterior border of the tubercle. (Reproduced, with permission, from Skinner HB. *Current Diagnosis and Treatment in Orthopedics*, 4th ed. New York, NY: McGraw-Hill; 2006. Figure 11-29.)

The **diagnosis of OSD can be made clinically**. The patient has no history of trauma, but he complains of knee pain that increases with exercise and trauma. Differential diagnosis of knee pain in adolescents includes a number of conditions. Patellofemoral stress syndrome, also common in athletes, causes chronic, dull, nonlocalizing knee pain. Jumper's knee (patellar tendonitis) is caused by microscopic patellar tendon injury; most affected patients have chronic, anterior knee pain and tenderness of the inferior portion of the patella. Iliotibial band friction syndrome causes lateral knee pain in runners. **Slipped capital femoral epiphysis (SCFE)** occurs in heavy **adolescents** during the growth spurt, leading to a limp and groin or thigh pain; however, hip pain may be referred to the knee. Examination of such patients reveals limited hip flexion, internal rotation, and abduction. Radiographs (anteroposterior and frog-leg views) of the hip reveal widening of the femoral epiphysis and osteopenia. Patients with SCFE are at risk for **avascular**

**necrosis** of the femoral epiphysis and require orthopedic evaluation. Other diagnoses to be considered in the adolescent with knee pain include trauma, tumor, leukemia, and septic joint.

Treatment of OSD consists of decreased activity. Ice after exercise and nonsteroidal anti-inflammatory drugs may provide some relief. In severe cases, knee immobilization and the use of crutches may be required. A trial of hyperosmolar dextrose injection for recalcitrant Osgood-Schlatter disease has shown some promise in one study. Symptoms may recur until ossification is complete. Long-term prognosis is excellent.

## COMPREHENSION QUESTIONS

- 53.1 A 12-year-old boy complains of right knee pain that is worse after he runs. His pain started 3 weeks after he joined the track team. He has tenderness of the tibial tubercle. Which of the following statements is accurate?
- A. A left shoe orthotic device will allow him to continue running and will alleviate the pain.
  - B. Decreasing his activity should alleviate the pain.
  - C. Initial therapy consists of immobilization.
  - D. The most likely cause of his pain is a stress fracture.
  - E. The most likely diagnosis is slipped capital femoral epiphysis.
- 53.2 A 13-year-old adolescent male has 1 week of limping and right knee pain. On your growth curve you determine that his weight is greater than the 95th percentile for age. His physical examination is remarkable for mild acanthosis and normal knees. His hip examination demonstrates diminished ability to flex and internally rotate his right femur. Which of the following is the best next step in management?
- A. Instruct the patient to rest and apply ice to the affected area.
  - B. Prescribe daily oral nonsteroidal anti-inflammatory drugs until the pain resolves.
  - C. Order a magnetic resonance imaging of the knee and hip.
  - D. Arrange for an orthopedic surgery consultation.

E. Prescribe a short course of oral steroids to decrease inflammation.

**53.3** A 14-year-old adolescent female arrives for a routine well-child evaluation. The mother reports that her daughter has previously been well, but she wants you to discuss the importance of sunscreen since she did not use sunscreen at a recent pool party and returned home 3 weeks ago with a sunburn across her cheeks and nose; the adolescent rolls her eyes at her mother. When the mother leaves the room the patient reports that she did use sunscreen but did not feel like arguing with her mother. She states that she has been well, but also notes that she has had 2 months of intermittent right knee pain that does not appear to be related to exercise. Upon further questioning she reports that she has not been feeling well and is increasingly tired. Your physical examination demonstrates the sunburn across the nose but no knee abnormalities and a normal gait. Which of the following is the most appropriate next step in management?

A. Prescribe ibuprofen and recommend daily sunscreen use.

B. Obtain radiographs of the knee.

C. Obtain further history with regard to fever, weight loss, rashes, and arthritis.

D. Recommend a knee immobilizer.

E. Arrange for an emergent orthopedic consultation for evaluation of possible SCFE.

**53.4** A 15-year-old adolescent male presents with right knee pain; he cannot bear weight on the affected joint. The knee is tender, edematous, warm, erythematous, and has significantly diminished range of motion. Which of the following is the best next step in his evaluation?

A. Obtain more history, including sexual history.

B. Prescribe a course of systemic steroids.

C. Administer intra-articular steroids to decrease inflammation.

D. Prescribe anti-inflammatory drugs.

E. Arrange for an outpatient orthopedic surgery consultation.

## ANSWERS

- 53.1 **B.** This boy's history is consistent with OSD. Initial therapy includes ice after exertion and rest.
- 53.2 **D.** The most likely diagnosis is SCFE. The patient is put on bed rest, and orthopedic surgery consultation is required.
- 53.3 **C.** This patient has complaints of joint pain and malaise, and she had a malar facial rash consistent with that of systemic lupus erythematosus (SLE). The next step is to obtain more history of other signs and symptoms of autoimmune disease, medication use (drug-induced SLE), and travel history (tick exposure for Lyme disease).
- 53.4 **A.** This patient has signs and symptoms of a septic joint. *Neisseria gonorrhoeae* is a major cause of septic arthritis in sexually active adolescents and young adults. If septic arthritis is suspected, immediate orthopedic evaluation and intravenous antibiotics are warranted.
- 

### CLINICAL PEARLS

- Osgood-Schlatter disease is found exclusively in young adolescents prior to closure of the growth plate.
  - Edema and tenderness of the tibial tuberosity are classic features of Osgood-Schlatter disease.
  - Slipped capital femoral epiphysis can cause limping and is most common in overweight adolescents.
- 

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## CASE 54

A 2-week-old male newborn presents with a “twisted neck.” He was born at term through a difficult vaginal delivery because of his large size (4550 g). On examination, his head is tilted toward the right side, his chin is rotated toward the left, and he has a palpable, firm, right sternocleidomastoid muscle mass.

► What is the most likely diagnosis?

► What is the best treatment?

## ANSWERS TO CASE 54: Torticollis

*Summary:* A 2-week-old large male born after difficult delivery has torticollis and a palpable sternocleidomastoid muscle mass.

- **Most likely diagnosis:** Muscular torticollis.
- **Best treatment:** Initially, passive stretching of the sternocleidomastoid muscle.

## ANALYSIS

### *Objectives*

1. Understand the common causes of torticollis.
2. Recognize the differences in treatment of torticollis based on the etiology.

### *Considerations*

This 2-week-old newborn had a difficult delivery because of his large size. He has torticollis (head tilted toward the right and chin rotated toward the left) as a result of decreased range of movement of the sternocleidomastoid muscle caused by the mass. Such infants are at increased risk for muscular torticollis because of sternocleidomastoid muscle injuries. Breech infants and those with hip dysplasia and metatarsus adductus also are at higher risk for torticollis.

APPROACH TO:

**Torticollis**

## DEFINITIONS

**KLIPPEL-FEIL SYNDROME:** Congenital fusion of portions of the cervical vertebrae, restricted neck movement, short neck, and low hairline. Associated features include Sprengel deformity (see below) and structural urinary tract abnormalities.

**SANDIFER SYNDROME:** Gastroesophageal reflux (GER), hiatal hernia, and posturing of the head.



**SPRENGEL DEFORMITY:** Congenital elevation of the scapula.

## CLINICAL APPROACH

**Torticollis**, identified in a patient with an **obviously twisted neck with the head tilted toward one side and the chin tilted toward the opposite side**, is commonly caused by injury and contracture of the **sternocleidomastoid muscle**. Torticollis presents at or soon after birth; infants may have experienced birth trauma and usually have a palpable, firm mass within the affected muscle. Cervical spine radiography is generally performed to rule out vertebral malformations.

If the spine is normal, therapy by the caregiver (and occasionally a physical therapist) involves **gentle sternocleidomastoid muscle stretching** (moving the head toward a neutral position). If the condition persists beyond the first months of life, an orthopedic consultation is indicated. **Persistent torticollis can lead to facial asymmetry.**

Congenital cervical vertebrae malformations can cause torticollis; gentle stretching does not improve the condition and may result in injury. Radiography demonstrates spinal anomalies such as hemivertebrae or areas of vertebral fusion or subluxation. **Klippel-Feil syndrome** can present as torticollis and includes congenital fusion of portions of the cervical vertebrae, restricted neck movement, short neck and low hairline, Sprengel deformity, and urinary tract abnormalities.

**Torticollis presenting beyond infancy requires cautious evaluation** because trauma and inflammation are common. Traumatic torticollis can occur following cervical vertebrae injury with subsequent fracture or atlanto-occipital, atlantoaxial, or C2–3 subluxation or injury to the cervical musculature; radiographic evaluation is essential. Inflammatory torticollis often follows an upper respiratory illness; muscular pain and tenderness and a normal neurologic evaluation are seen. Other inflammatory causes include cervical lymphadenitis, retropharyngeal abscess, cervical vertebral osteomyelitis, rheumatoid arthritis, and upper lobe pneumonia. Children with cervical lymphadenitis are generally afebrile and have palpable, tender cervical lymph nodes. Patients with retropharyngeal abscess may present with fever, dysphagia, dyspnea, drooling, or stridor secondary to compression.

A variety of neurologic conditions cause torticollis: Down syndrome, visual disturbances, dystonic reactions to medications (phenothiazine, haloperidol, or metoclopramide), spinal cord or posterior fossa tumors, syringomyelia, Wilson disease, dystonia musculorum deformans, and spasmus nutans. A physical examination with particular attention to the neurologic examination may identify findings associated with one of these neurologic causes. Miscellaneous causes include cervical disc calcification, Sandifer syndrome, benign paroxysmal torticollis, bone tumors, soft-tissue tumors, and hysteria.

## COMPREHENSION QUESTIONS

- 54.1 A 3-month-old male infant has intermittent neck contortions and arching. He was term at birth, with an uneventful prenatal course and delivery. He frequently spits up after feeding, and has had one episode of pneumonia. Which of the following is the best next step in management?
- A. Begin gentle stretching of the sternocleidomastoid muscle.
  - B. Evaluate him for gastroesophageal reflux disease (GERD).
  - C. Refer him for orthopedic evaluation.
  - D. Obtain cervical spine radiographs.
  - E. Observe and, if the condition persists, refer him for orthopedic evaluation.
- 54.2 A 5-month-old female infant presents with sudden onset of torticollis and facial grimacing, but otherwise she appears alert and interactive. She has been doing well and has gained weight for the last month after having been prescribed ranitidine and metoclopramide for GERD. Which of the following statements is accurate?
- A. She is likely having a partial-complex seizure and needs an electroencephalograph.
  - B. A lumbar puncture for cell count, glucose, and protein is warranted.
  - C. Measurement of serum electrolyte and glucose levels is unnecessary.
  - D. She is likely having a dystonic reaction to one of her medications.
  - E. A cervical spine magnetic resonance image is likely to show a congenital abnormality.

- 54.3 A 6-year-old boy presents with torticollis, fever, sore throat, and difficulty swallowing solids and liquids but no drooling. He denies headache and dyspnea, and he remains only somewhat playful. Examination reveals posterior pharyngeal edema. Which of the following is the best next step in management?
- A. Examine his cerebrospinal fluid.
  - B. Obtain imaging studies of the airway and soft tissues of the neck.
  - C. Send a throat culture and begin antibiotic therapy based on the results.
  - D. Begin oral penicillin.
  - E. Prescribe ibuprofen and neck stretching exercises.
- 54.4 A 1-week-old female newborn presents with her new adoptive parents. The family complains that she seems to have a twisted neck. They know only that “delivery was almost a C-section because the baby was lying sideways.” She has been feeding well and has had appropriate urine and stool output for the last 24 hours. Physical examination is significant for torticollis. Which of the following statements is most accurate?
- A. She is at significant risk for aspiration pneumonia.
  - B. The parents should immediately begin a regimen of gentle stretching of the neck.
  - C. Radiographs of the cervical spine should be obtained.
  - D. Immediate orthopedic consultation should be arranged.
  - E. Immediate neurologic consultation should be arranged.

## ANSWERS

- 54.1 **B.** This infant most likely has GER with intermittent torticollis (Sandifer syndrome). He has a history of frequently spitting up and has had pneumonia (possibly aspiration), indicating he has GER. Sandifer syndrome infants have abnormal head posturing associated with reflux. The head movements are thought to occur in response to pain or to protect the airway.
- 54.2 **D.** This infant has sudden onset of the dystonic features of torticollis and facial grimacing, most likely as a result of the metoclopramide. However,

initial evaluation for seizures, including measurement of serum electrolyte, glucose, and calcium levels, is indicated. Diphenhydramine administration may rapidly reverse this drug-induced dystonia. An MRI is unlikely to demonstrate a cervical abnormality because the symptom onset was abrupt. Cerebrospinal fluid analysis as a first step likely will not result in determination of the cause of this type of torticollis.

**54.3 B.** This child has signs and symptoms of retropharyngeal cellulitis or abscess. Such patients may have fever, dysphagia, drooling, stiff neck, dyspnea, or airway stridor. Physical findings include midline or unilateral swelling that may become a fluctuant mass. Management includes antibiotic therapy with possible incision and drainage of the abscess. Computed tomography may be helpful in early identification of abscess formation.

**54.4 C.** This child appears to have had a difficult delivery, making muscular torticollis likely. If cervical spine radiography is normal, the parents can begin gentle stretching to move the head in a neutral position. If the condition persists, orthopedic referral is necessary.

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### CLINICAL PEARLS

- Muscular torticollis is most commonly found in infants as a result of sternocleidomastoid muscle trauma.
  - Sandifer syndrome is characterized by gastroesophageal reflux and posturing of the head.
  - Drug-induced dystonia is most frequently caused by phenothiazine, metoclopramide, and haloperidol.
- 

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## CASE 55

A full-term infant is delivered vaginally after a pregnancy that was uncomplicated. On initial examination it is noted that the baby has cloudiness of both lenses, which obscures the red reflex. The family history is significant for the father having had eye surgery at a young age. The physical examination otherwise is unremarkable.

- What is the most likely diagnosis?
- What is the next step?

### ANSWERS TO CASE 55: **Congenital Cataracts**

*Summary:* A healthy full-term infant with bilateral lens cloudiness and a family history of ophthalmologic condition requiring surgery.

- **Most likely diagnosis:** Congenital cataracts.

- **Next step:** Ophthalmologic evaluation and complete evaluation for possible associated hereditary, metabolic, or infectious causes.

## ANALYSIS

### *Objectives*

1. Understand the conditions associated with congenital cataracts.
2. Understand the development of amblyopia.

### *Considerations*

This newborn presents with an isolated eye finding consistent with cataracts and a positive family history of eye disease. It is important to assess the infant for common chromosomal, metabolic, and infectious entities associated with congenital cataracts.

### APPROACH TO:

#### **Congenital Cataracts**

## DEFINITIONS

**Cataract:** Opacity of the lens. Depending on the size and location, the cataract may affect vision.

**Aphakia:** Absence of the lens.

**Amblyopia:** Loss of vision caused by underuse of one eye.

## CLINICAL APPROACH

Congenital cataracts occur in approximately 2 of 10,000 births. They are an isolated condition in 50% to 60% of cases and part of a syndrome in 20% to 25% of cases. Many of the cases of isolated congenital cataracts are hereditary in origin, with most being transmitted through autosomal dominance. Developmental cataracts may result from prenatal infections, such as toxoplasmosis, cytomegalovirus, syphilis, rubella, and herpes simplex virus, or secondary to metabolic diseases such as **galactosemia**, homocystinemia, galactokinase deficiency, abetalipoproteinemia, Fabry,

Hurlers, Nieman-Pick, Refsum, and Wilson. Intraocular abnormalities including retinopathy of prematurity, retinitis pigmentosa, uveitis, and retinal detachment may lead to the development of cataracts. Chromosomal anomalies associated with cataracts include trisomies 13, 18, and 21; Turner syndrome; and various depletion and duplication syndromes.

Evaluation of infants presenting with congenital cataracts includes physical examination, assessment of TORCH titers, evaluation for galactosemia (part of the newborn metabolic screening test), a full ophthalmologic examination, and ocular ultrasound in cases with completely opaque lenses. Parents should also have full dilated ophthalmologic evaluation including slit lamp examination.

If visual disturbance is significant, surgical removal of lens is performed. Surgery may occur as early as 2 to 4 weeks after birth. The infant is then fitted with refraction contact lens; intraocular lens placement is used in older children and has recently been used in children under 2 years of age. Infants with unilateral cataracts without surgery may need patching of their good eye to prevent the development of deprivation amblyopia.

In addition to deprivation amblyopia (opacity in the visual axis), other forms of amblyopia include strabismic (poorly formed image due to deviated eye), ametropic (high refractive error in both eyes), and anisometropic (unequal vision between the eyes). For all of these lesions, the common cause of pathology for the child is interference with the development of clear images during the critical period of eye development in infancy and early childhood. Amblyopia is usually asymmetric and is diagnosed when an ophthalmologic examination demonstrates reduced acuity otherwise not explained by an organic etiology. Early detection of this condition is key since recovery of eye function is more likely the younger the child.

Treatment for amblyopia must first include removal of any opacity and then ensuring well-focused retinal images are being produced in each eye; glasses may be necessary. Strengthening of the “weak” eye is accomplished by covering the “good” eye (occlusion therapy) or using eye drops in the “good” eye (penalization therapy). Close monitoring by a pediatric ophthalmologist will ensure that the treatment maximizes the benefits to the amblyoptic eye while not causing amblyopia to develop in the nonaffected eye.

## COMPREHENSION QUESTIONS

- 55.1 A full-term, small for gestational age newborn girl presents with cataracts, petechiae, and a continuous machine-like murmur. Which of the following statements is accurate?
- A. This infant needs an audiology evaluation as sensorineural hearing loss is a common association.
  - B. This infant needs a renal ultrasound as she is likely to have renal abnormalities.
  - C. Treatment of her condition includes 14 days of intravenous penicillin after evaluation of her cerebrospinal fluid.
  - D. The infant's condition is likely to have occurred due to a maternal illness during the third trimester.
  - E. Intravenous antiviral therapy should be initiated and viral cultures should be obtained.
- 55.2 A healthy 2-week-old girl has yellow discharge from her left eye. Her mother had early prenatal care, the baby was delivered vaginally, and she was discharged at 48 hours of life. Within the first few days of life, the mother noted that the baby had increased tear production in her left eye, which now has yellow discharge. She has red reflexes bilaterally, her pupils are equal and reactive to light, and she has no scleral injection. She has left-sided mucous ocular discharge. The next step is to:
- A. Administer intravenous antibiotic therapy.
  - B. Begin a course of oral antimicrobial treatment.
  - C. Begin a course of topical antimicrobial treatment and nasolacrimal massage and warm water cleansing.
  - D. Incise and drain the area.
  - E. Refer the child for an outpatient ophthalmologic evaluation.
- 55.3 A 4-month-old infant has excessive right-sided tearing. His mother states he becomes irritable in bright light and calms in a darkened room. On examination, he has eye asymmetry, with the right eye appearing to be larger than the left. Which of the following statements is accurate?



- A. Warm compresses and gentle massage are first-line therapy.
- B. In most cases, treatment is nonsurgical.
- C. The infant has the classic features of Down syndrome.
- D. Immediate systemic antibiotic therapy will reduce complications.
- E. Immediate referral to a pediatric ophthalmologist is warranted.

## ANSWERS

- 55.1 A. This infant has the classic features of congenital rubella syndrome including low birth weight, heart defect (patent ductus arteriosus), and congenital cataracts. Other clinical findings associated with congenital rubella syndrome include purpura, hepatosplenomegaly, jaundice, retinopathy, glaucoma, pulmonary artery stenosis, meningoencephalitis, thrombocytopenia, and hemolytic anemia. Long-term sequelae of congenital rubella include sensorineural hearing loss, neurodevelopmental abnormalities, endocrine disease, and hypogammaglobulinemia. Maternal infection may or may not be clinically apparent, and infection during the first month is most likely to result in fetal infection with the involvement of multiple organs.
- 55.2 C. This infant had excessive tear production that later became a mucopurulent discharge but had an otherwise normal ophthalmologic examination. Of note, the conjunctiva is not inflamed and the cornea is not involved. Initial treatment includes topical antibiotic therapy and nasolacrimal duct massage two to three times daily with warm water eyelid cleansing.
- 55.3 E. A history of excessive tearing and photophobia and examination findings of corneal enlargement suggest an **immediate** evaluation for congenital glaucoma is indicated as treatment is surgical. **Infantile glaucoma** occurs in 1 in 100,000 births with a **classic triad of tearing, photophobia, and blepharospasm**. It may be isolated or occur with various conditions, including congenital rubella, neurofibromatosis type 1, mucopolysaccharidosis I, Lowe oculocerebrorenal syndrome, Sturge-Weber syndrome, Marfan syndrome, and several chromosomal abnormalities. The increased intraocular pressure can lead to expansion of the globe and corneal damage.

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## CLINICAL PEARLS

- Galactosemia is associated with cataracts.
  - Workup of an infant with congenital cataract includes TORCH titers.
  - Amblyopia must be diagnosed at an early period so that occlusive or penalization therapy may be instituted on the unaffected eye to maximize improvement to the vision on the affected eye.
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## CASE 56

A 13-month-old boy presents because his parents are concerned that he does not speak recognizable words, has never made babbling sounds such as “baba” or “dada,” does not follow verbal commands, and does not respond to his name. He is appropriately affectionate and makes good eye contact with both of his parents. The child was a full-term baby without hospitalizations or frequent illnesses. He sat without support at 6 months and began walking at 11 months. He is active in the examination room, but he does not respond to his name or to verbal cues from his mother. He is a well-developed, well-nourished normal child otherwise.

► What is the most likely diagnosis?

► What is the next step?

### ANSWERS TO CASE 56: **Severe Hearing Loss**

*Summary:* A 13-month-old healthy boy has severe language delay but normal motor development.

- **Most likely diagnosis:** Hearing loss.
- **Next step:** Audiologic evaluation.

## ANALYSIS

### *Objectives*

1. Understand the major types of hearing loss.
2. Be aware of common causes of hearing loss.

### *Considerations*

This 13-month-old boy has never made babbling sounds such as “baba” and “dada,” which are the normal precursors to language development and usually

are seen by 9 months of age. His history and physical examination do not lead to a specific reason for this speech delay (eg, global developmental delay, syndromic features, or history of prematurity with associated morbidity). The next step is an audiology evaluation.

APPROACH TO:

**Hearing Loss**

## DEFINITIONS

**CONDUCTIVE HEARING LOSS:** Hearing loss caused by disorders of the outer ear (external auditory canal atresia and otitis externa) or middle ear (otitis media and cholesteatoma).

**RETROCOCHLEAR (CENTRAL) HEARING LOSS:** Hearing loss caused by deficits in the auditory nerve or central auditory nervous system.

**SENSORINEURAL HEARING LOSS (SNHL):** Hearing loss caused by cochlea disorders (damage from infection, noise, ototoxic agents, or genetic defects).

## CLINICAL APPROACH

Hearing can be divided into several categories ranging from normal hearing (threshold 0-15 decibels [dB]) to profound hearing loss (>70 dB). With mild hearing loss (25-30 dB), inability to hear some speech sounds is noted; with moderate hearing loss (30-50 dB), most normal speech is indiscernible. One to two newborns per 1000 live births have moderate to profound bilateral SNHL.

**Sensorineural hearing loss can be congenital or acquired.**

Approximately half of SNHL cases result from **genetic factors**. The hearing loss may be isolated (70%) or occur with other syndromic anomalies. The most **common autosomal dominant syndromes** associated are **Waardenburg syndrome types I and II** (partial albinism [often a white forelock], deafness, lateral displacement of the inner canthi, heterochromic irises, eyebrow confluence, and a broad nasal bridge) and **branchio-oto-renal syndrome** (hearing impairment, preauricular pits, branchial fistulas, renal impairment,

and external ear abnormalities). Other entities include Alport syndrome (nephritis, progressive renal failure, SNHL, ocular abnormalities), Down syndrome, neurofibromatosis, Jervell and Lange-Nielsen (prolonged QT) syndrome, and Hunter-Hurler syndrome. Ophthalmic or craniofacial abnormalities, external ear malformations, and metabolic, neurologic, or musculoskeletal disorders may be associated with SNHL.

**Prenatal cytomegalovirus (CMV) infection is the most common infectious cause of congenital SNHL;** it can cause hearing loss later in infancy and childhood. Toxoplasmosis, rubella, and syphilis can lead to congenital SNHL; ongoing hearing evaluations are important. Postnatal infections associated with acquired SNHL include group B streptococcal sepsis and *Streptococcus pneumoniae* meningitis. *Haemophilus influenzae* meningitis, mumps, measles, and rubella were common causes prior to current vaccination practices.

Conditions in the prenatal period that are associated with SNHL include prematurity, low birthweight (<1500 g), low Apgar score (0-4 at 1 minute or 0-6 at 5 minutes), mechanical ventilation greater than 5 days, hyperbilirubinemia, bacterial meningitis, ototoxic drug exposure, and craniofacial anomalies. Pharmacologic and chemical exposures can cause SNHL. Aminoglycosides, loop diuretics, chemo-therapeutic agents (cisplatin), isotretinoin, lead, arsenic, and quinine may cause SNHL with *in utero* or postnatal exposure. Other causes include temporal bone fractures, head trauma, extracorporeal membrane oxygenation (ECMO), radiation, and prolonged exposure to loud noise.

Early diagnosis of hearing impairment can impact development of communication skills. Hearing adequacy is evaluated at medical visits by asking parents about their baby's response to sounds and their baby's early language development. Universal newborn hearing screening through otoacoustic emissions (OAE) or auditory brain-stem-evoked responses (ABRs) is now recommended and is required by most states; the goal is hearing loss diagnosis prior to the age of 3 months and intervention before the age of 6 months. **Early intervention is believed to enhance communication skills and academic performance.**

Various hearing screening methods are used, depending on the child's developmental level and degree of hearing loss. Auditory brainstem-evoked response testing, often used as the diagnostic test of choice for the mandatory screening in newborns, measures electrophysiologic response and does not

require cooperation. Otoacoustic emissions are absent if the hearing threshold is above 30 to 40 dB. Infants through young preschool children can be assessed via visual reinforcement audiometry, behavioral audiometry, or play audiometry; these methods reveal information specific to each ear. In cooperative children, air conduction audiometry can be performed, using headphones and pure tones between 250 and 8000 Hz. The same sounds are presented through oscillator, usually on the mastoid, thus evaluating bone conduction.

Children with SNHL are evaluated by an otolaryngologist, an audiologist, and a speech pathologist. Children with SNHL have a small increased risk for otogenic meningitis and need careful attention to vaccination against *Streptococcus pneumoniae*. Patients with mild to moderate hearing loss can benefit from hearing aids, which can be fitted in infants as young as 2 months. With severe and profound hearing loss, a combination of hearing aids, sign language, lip reading, and attention to appropriate educational surroundings is used. Cochlear implantation is a treatment option for selected children.

## COMPREHENSION QUESTIONS

- 56.1 A 26-month-old boy presents because of maternal concern about his hearing. Over the past few weeks, his mother has had to speak more loudly in order for him to respond. He has a greater than 50-word vocabulary and can put together 2- to 3-word sentences. Three weeks prior he had an upper respiratory infection (URI). Which of the following is the best next step in treatment?
- A. Order ABR testing.
  - B. Perform otoscopy with insufflation.
  - C. Send him for a complete audiologic evaluation.
  - D. Perform hearing screening in the clinic.
  - E. Explain to the mother that 2-year-old children often do not respond to their parents.
- 56.2 A 4-month-old boy has a white forelock, a broad mandible, and lateral displacement of his inner canthi. His mother also has a white forelock. Which of the following statements is true?
- A. A urinalysis will demonstrate increased protein levels.

- B. He is not at risk for hearing loss if his mother has normal hearing.
  - C. He is at risk for SNHL; order an audiologic evaluation.
  - D. The inheritance pattern of this disorder is X-linked recessive.
  - E. He should have ongoing clinic hearing screening with referral for formal hearing if abnormalities are detected.
- 56.3 Which of the following groups of children is at especially high risk for hearing loss?
- A. A full-term, large-for-gestational-age male born to a mother with gestational diabetes
  - B. An appropriate-for-gestational-age (AGA) infant, the product of a 34-week pregnancy, who had Apgar scores of 7 and 8 at 1 and 5 minutes, respectively
  - C. A term, 3300-g infant born by cesarean section who had a peak total bilirubin level of 15 mg/dL at 72 hours of life
  - D. A term AGA baby who received cefotaxime and ampicillin for 48 hours for suspected sepsis
  - E. A term AGA infant born by cesarean section for placental abruption with Apgar scores of 3 and 5 at 1 and 5 minutes, respectively
- 56.4 Which of the following would be the expected language development of a normal 24-month-old child?
- A. Speech that is 90% understandable
  - B. A 10-word vocabulary but no combination of words
  - C. A 50-word vocabulary and 2-word combinations to make a sentence
  - D. Appropriate use of pronouns
  - E. A 200-word vocabulary and 4- to 5-word combinations to make a sentence

## ANSWERS

- 56.1 **B.** This child has normal speech development and was recently noted to have a possible hearing deficit. With the recent URI, he is at risk for otitis media with effusion and conductive hearing loss. Otoscopy with

insufflation (gently blowing air into the ear canal to determine tympanic membrane movement) is helpful for qualitative evaluation of middle ear effusion. Tympanometry is a reliable, quantitative tool for assessing middle ear effusion. If he has conductive hearing loss, further evaluation is indicated.

- 56.2 C. This child has features of Waardenburg syndrome (partial albinism, often a white forelock, SNHL, lateral inner canthi displacement, eyebrow confluence, and a broad nasal bridge and mandible); inheritance is autosomal dominant. Children with syndromic features strongly associated with hearing loss require hearing evaluation.
- 56.3 E. Infants born with Apgar scores of 4 or less at 1 minute and 6 or less at 5 minutes require audiologic evaluation. Other infants who should undergo testing include those with a family history of childhood SNHL; cytomegalo-virus, rubella, syphilis, herpes, or toxoplasmosis infection; craniofacial anomalies; birth weight less than 1500 g; hyperbilirubinemia at a level requiring exchange transfusion; bacterial meningitis; mechanical ventilation for more than 5 days; and stigmata of syndromes associated with hearing loss, especially those with renal abnormalities.
- 56.4 C. At 24 months of age, the average child has a vocabulary of approximately 50 words and forms 2-word sentences. A 12-month-old child has a vocabulary of 2 to 4 words in addition to appropriately saying “mama” and “dada.” By 36 months, a child should have a vocabulary of 250 words, produce at least 3-word sentences, and use pronouns.

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### CLINICAL PEARLS

- ▶ Cytomegalovirus infection is the most common infectious cause of congenital sensorineural hearing loss.
- ▶ Aminoglycosides and loop diuretics may cause sensorineural hearing loss.
- ▶ Syndromes associated with renal abnormalities have a higher incidence of hearing loss.

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Universal hearing screening at birth is recommended.



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### CASE 57

A previously healthy 3-year-old boy presents with sudden onset of rash. His mother says he had been playing when she noticed small red spots and a large purple area on his skin. He has had no fever, upper respiratory tract infection (URI) symptoms, weight loss, bone pain, or diarrhea, and he is not taking medications. Three weeks previously, he had a mild illness that self-resolved after 48 hours. He is playful on examination, but he has multiple petechiae and purpuric lesions on his upper and lower extremities and on his trunk. He has neither adenopathy nor splenomegaly. His white blood cell (WBC) count is  $8500/\text{mm}^3$ , hemoglobin level is 14 mg/dL, and his platelet count is  $20,000/\text{mm}^3$ .

- ▶ What is the most likely diagnosis?
- ▶ What is the next step in management?

### ANSWERS TO CASE 57: **Immune Thrombocytopenic Purpura**

*Summary:* A healthy 3-year-old develops thrombocytopenia, petechiae, and purpuric lesions. He is well-appearing but recently had a febrile illness. His WBC count and hemoglobin levels are normal.

- **Most likely diagnosis:** Immune thrombocytopenic purpura (ITP).
- **Next step in management:** Evaluation of his peripheral blood smear.

## ANALYSIS

### *Objectives*

1. Know the most common causes of childhood thrombocytopenia.
2. Understand the natural history of ITP.

### *Considerations*

This 3-year-old has purpuric lesions and petechiae resulting from thrombocytopenia. He lacks the systemic signs of illness expected with disseminated intravascular coagulation or hemolytic-uremic syndrome (HUS). Because his hemoglobin level and WBC count are normal, bone marrow infiltration is less likely the cause of his thrombocytopenia. A peripheral blood smear is examined to identify immature WBCs and red cell morphology. Children with ITP have normal peripheral blood smears without evidence of leukemic or microangiopathic processes. This child has a platelet count of  $20,000/\text{mm}^3$  and lacks evidence of active bleeding; the next step is close observation.

APPROACH TO:

**Thrombocytopenia**

## DEFINITIONS

**HEMOLYTIC-UREMIC SYNDROME (HUS):** A syndrome of nephropathy, thrombocytopenia, and microangiopathic hemolytic anemia. It is associated with *Escherichia coli* 0157:H7, *Shigella*, and *Salmonella*. A prodrome of bloody diarrhea is common.

**HENOCH-SCHÖNLEIN PURPURA (HSP):** A syndrome of small-vessel vasculitis in young children. The syndrome may have dermatologic (petechial/purpuric rash), renal (nephritis), gastrointestinal (abdominal pain, gastrointestinal bleeding, intussusception), and joint involvement (arthritis).

**IMMUNE THROMBOCYTOPENIC PURPURA (ITP):** A condition of increased platelet destruction by circulating antiplatelet antibodies, most frequently antiglycoprotein IIb/IIIa.

## CLINICAL APPROACH

**Acute ITP is the most common cause of thrombocytopenia in a well child usually aged 2 to 10 years.** The evidence suggests an immunologic etiology triggered by a preceding viral illness, but the specific pathophysiologic mechanism is unknown. Acute ITP occurs with an equal gender distribution. Young children usually present with acute onset of petechiae and purpura and a history of a viral illness 1 to 4 weeks previously. Bleeding from the gingivae and other mucous membranes may occur. Examination findings include petechiae and purpura, especially in trauma areas. If significant lymphadenopathy or organomegaly is found, other causes for thrombocytopenia are considered.

Laboratory findings include thrombocytopenia, which can be severe ( $<20,000/\text{mm}^3$ ), but the platelet size is normal or increased. The WBC count and hemoglobin level are normal (unless excessive bleeding has occurred). Prothrombin time (PT) and activated partial thromboplastin time (aPTT) are normal. The peripheral blood smear may reveal eosinophilia or atypical lymphocytes; immature WBCs and abnormal red cell morphology are absent. Generally, bone marrow aspiration is unnecessary. If the peripheral blood smear is concerning, the WBC count is abnormal, or adenopathy or organomegaly is present, **bone marrow evaluation** aids in proper diagnosis, demonstrating an **increased number of megakaryocytes** in ITP. Within a month of presentation, more than half of untreated children have complete

resolution of their thrombocytopenia and up to another 30% have resolution by 6 months. Persistence beyond 6 months is considered chronic ITP.

The **most serious ITP complication, intracranial hemorrhage**, occurs in less than 1% of affected children. Patients with severe thrombocytopenia ( $<20,000/\text{mm}^3$ ), extensive mucosal bleeding, severe complications (eg, massive gastrointestinal bleeds), or without a protective environment may require medical intervention. Treatment to decrease platelet destruction includes **intravenous immunoglobulin** for 1 to 2 days, **intravenous anti-D therapy**, or a 2- to 3-week course of **systemic corticosteroids**. Platelet transfusion is reserved for life-threatening bleeding. **Splenectomy** may be considered in children with **serious complications not responding to other therapies**. After splenectomy, **pneumococcal vaccine and penicillin prophylaxis** are required because of risk for sepsis.

**From 10% to 20% of ITP patients have chronic thrombocytopenia lasting for more than 6 months**, occurring more commonly in older children and in females; it may be part of other autoimmune disease or may occur with infection such as human immunodeficiency virus (HIV) or Epstein-Barr virus (EBV). The ITP treatment options listed above are available for chronic ITP patients; the goal remains prevention of serious thrombocytopenia complications.

Many pharmacologic agents may cause immune-mediated thrombocytopenia, including penicillins, trimethoprim-sulfamethoxazole, digoxin, quinine, quini-dine, cimetidine, benzodiazepine, and heparin. The measles, mumps, and rubella (MMR) vaccine is associated with thrombocytopenia and is used cautiously in ITP patients.

## COMPREHENSION QUESTIONS

**57.1** A 2-year-old girl has a rash. She was well until 2 weeks prior when she had fever and URI symptoms that resolved without treatment. On examination, she has petechiae on her upper and lower extremities and trunk. Her platelet count is  $25,000/\text{mm}^3$ . Her WBC count is  $9000/\text{mm}^3$  and hemoglobin level is 11 mg/dL. Which of the following is the best next step in management?

A. Obtain a review of the peripheral blood smear.

- B. Administer intravenous immunoglobulin.
- C. Send a blood culture and begin empiric antimicrobial therapy.
- D. Order a platelet transfusion.
- E. Arrange for bone marrow biopsy.

**57.2** A 14-year-old adolescent female has a rash on her arms and legs. She was diagnosed with a urinary tract infection 4 days ago, which is being treated with trimethoprim-sulfamethoxazole. She denies fever, vomiting, diarrhea, headache, and dysuria. On examination she has multiple upper- and lower-extremity petechiae. Her WBC count is  $7000/\text{mm}^3$  and hemoglobin level is 13 mg/dL; her platelet count is  $35,000/\text{mm}^3$ . Which of the following is the best next step in management?

- A. Send blood for antinuclear antibody (ANA).
- B. Send a repeat urinalysis.
- C. Discontinue the trimethoprim-sulfamethoxazole.
- D. Obtain HIV testing.
- E. Administer intravenous immunoglobulin.

**57.3** A 7-year-old boy has a rash on his lower extremities and pain in his right knee. He has had a low-grade fever and abdominal pain, and he has felt tired. He is nontoxic appearing, but he has palpable petechiae on his lower extremities and buttocks. His right knee is mildly edematous and he can bear weight on his right leg, but complains of pain. His prothrombin time (PT), partial thromboplastin time (PTT), and platelet counts are normal. Which of the following is the best next step in management?

- A. Begin a course of systemic corticosteroids.
- B. Begin empiric antimicrobial therapy for sepsis.
- C. Obtain a urinalysis and provide supportive care.
- D. Perform aspiration of the synovial fluid in his right knee.
- E. Administer intravenous immunoglobulin.

**57.4** A 3-year-old boy has pallor, lethargy, and decreased urine output. He was well until the preceding week, when he had fever, vomiting, and bloody diarrhea (now resolved). On examination, he is lethargic and has

hepatosplenomegaly and scattered petechiae. Urinalysis reveals hematuria and proteinuria. Which of the following statements about his condition is accurate?

- A. A complete blood (cell) count (CBC) is likely to reveal thrombocytosis.
- B. Initial therapy includes systemic corticosteroids.
- C. Empiric antimicrobial therapy for sepsis should be initiated.
- D. An emergent oncology consultation for probable leukemia should be arranged.
- E. Peripheral blood smear is likely to reveal helmet cells and burr cells.

## ANSWERS

- 57.1 A. This child has the classic ITP features of isolated thrombocytopenia in a well-appearing child. An examination and peripheral blood smear are necessary. If no lymphadenopathy or organomegaly is found and the peripheral blood smear is normal, initial management includes close observation and a protective environment.
- 57.2 C. The thrombocytopenia may be the result of the trimethoprim-sulfamethoxazole; the medicine is discontinued and her platelet count is monitored. If thrombocytopenia continues, she may have ITP and is followed for chronic ITP. Chronic ITP occurs in older children (female predominance); it may be seen with autoimmune disease such as systemic lupus erythematosus or with chronic infections including HIV.
- 57.3 C. This child has signs and symptoms of HSP, a vasculitis of the small vessels with renal, gastrointestinal, joint, and dermatologic involvement. Initial therapy consists of hydration and pain control. With renal involvement, urinalysis reveals red blood cells (RBCs), WBCs, casts, or protein. Gastrointestinal complications include hemorrhage, obstruction, and **intussusception**(see Case 49, Question 49.4 for more discussion about intussusception); abdominal pain requires careful evaluation.
- 57.4 E. This child has features of HUS, which frequently follows a bout of gastroenteritis; it has been associated with *E coli* 0157:H7, *Shigella*, and *Salmonella*. Patients have pallor, lethargy, and decreased urine output;

some have hepatosplenomegaly, petechiae, and edema. Laboratory findings include hemolytic anemia and thrombocytopenia; peripheral blood smear demonstrates helmet cells, burr cells, and fragmented RBCs. Acute renal failure is manifested by hematuria, proteinuria, and an elevated serum creatinine level. Management is supportive with careful monitoring of renal and hematologic parameters; dialysis may be required.

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## CLINICAL PEARLS

- Idiopathic thrombocytopenic purpura is the most common cause of acute thrombocytopenia in a well young child.
  - Approximately 70% to 80% of children with idiopathic thrombocytopenic purpura have spontaneous resolution within 6 months.
  - Hemolytic-uremic syndrome consists of nephropathy, thrombocytopenia, and microangiopathic hemolytic anemia; it is associated with *E coli* 0157:H7 and *Shigella*.
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## CASE 58

A 4-month-old boy presents with irritability for 2 days. He lives with his mother, 21-month-old sister, and 3-year-old brother. On physical examination, the infant has right thigh swelling and tenderness. Radiographs of the right lower extremity reveal a femur fracture.

- What is the most likely diagnosis?
- What is the next step in the management of this child?

## ANSWERS TO CASE 58: **Child Abuse**

*Summary:* A 4-month-old boy presents with a 2-day history of irritability. The infant has no history of trauma. A right transverse femur fracture is present.



- **Most likely diagnosis:** Physical abuse.
- **Next step:** Obtain a skeletal survey.

## ANALYSIS

### *Objectives*

1. Understand the importance of reporting suspected child maltreatment.
2. Recognize that child abuse is suspected if significant inconsistencies exist between the physical injury and the trauma history. It is imperative that the child's developmental level be assessed in regard to the child's possible role in an accidental injury.

### *Considerations*

The lack of trauma history is very concerning in this infant who is not mobile. The mother's delay in seeking medical care for 2 days from symptom onset is concerning. Cases of suspected abuse are reported to Child Protective Services (CPS) or law enforcement. Thus, the next steps are to obtain a complete skeletal survey to detect other bony injuries and to report this child's possible abuse case to CPS.

APPROACH TO:

**Child Abuse**

## DEFINITIONS

**CHILD PROTECTIVE SERVICES (CPS):** Local governmental agency responsible for investigating suspected child maltreatment cases.

**MUNCHAUSEN SYNDROME BY PROXY:** Abuse in which the caretaker falsifies symptoms or inflicts injury upon a child to necessitate medical intervention.

**ABUSIVE HEAD TRAUMA (SHAKEN BABY OR SHAKEN IMPACT SYNDROME):** Brain injury resulting from violent shaking of the infant or shaking the infant followed by collision of the head against a hard surface. Infants may present with seizures, respiratory arrest, a bulging fontanelle, or irritability. Intracranial injury is found with computed tomography (CT) or

magnetic resonance image (MRI), and **retinal hemorrhages** may be visualized on funduscopy. Skeletal injuries such as rib fractures or classic metaphyseal lesions may also be present.

## CLINICAL APPROACH

Child maltreatment is common, with approximately 1 million substantiated cases per year in the United States. Child maltreatment includes neglect and physical, sexual, and emotional abuse; children often suffer from more than one type. **Neglect is the most common form of child maltreatment and consists of failure to provide adequate nutrition, shelter, supervision, or medical care.** Physical abuse accounts for approximately 20% of cases, occurring when caregivers inflict excessive physical injury. Although the definition of “appropriate” corporal punishment is argued, physical abuse is considered when marks (eg, bruising, lacerations, burns, or fractures) result. Sexual abuse occurs in 10% of substantiated maltreatment cases.

Munchausen syndrome by proxy is a less common form of child abuse. Affected children are hospitalized repeatedly with undiagnosed or vague conditions. Children may also have underlying medical conditions with abnormally frequent or persistent symptoms. The hospitalization is remarkable for a caretaker who takes great interest in the medical staff and interventions and often times has some type of medical background. The caretaker forms relationships with health-care providers and is often noted to be an exemplary parent. Munchausen syndrome by proxy ranges from fabricating symptoms to actual poisoning or suffocations.

Reporting of cases of child maltreatment has been mandated since the 1960s, resulting in increased public and medical awareness. Health-care providers legally are required to report suspected abuse to CPS or law enforcement.

Medical evaluation of suspected child maltreatment cases includes obtaining a medical history and a family assessment, conducting a thorough physical examination, obtaining appropriate diagnostic testing, and interviewing the child and the family. Routine medical history includes information about illnesses, hospitalizations, injuries, and pertinent family history. History should be carefully documented within the medical record as discrepancies to different providers or by different caretakers may provide

vital information. A **developmental history** helps determine if the events described by a family are a plausible explanation for injuries found (eg, a 10-month-old child is unable to climb into a bathtub, turn on the water, and sustain second-degree burns only to the buttocks). Documentation must include who lives in the home and who provides care for the child.

An examination is performed with attention to any skin lesions. Body charts (or photographs) assist in documenting the injuries. **A skeletal survey (skull, chest, spine, and limbs) assists in obtaining evidence of prior trauma in children younger than 3 years.** Recent fractures may not be detectable on plain radiographs for 1 to 2 weeks after an injury; if necessary, bone scans demonstrate fractures within 24 to 48 hours of injury. Children with bruising often may be evaluated with a platelet count and coagulation studies to eliminate hematologic disorders as a cause.

Although bruises and lacerations are common abuse indicators, they also are common in nonabused children. **Accidental bruises are usually found over bony areas** (knees, shins, elbows, forehead) and are appropriate for the child's developmental milestones. **Abdomen, buttocks, thighs, and inner arm bruises occur less frequently in cases of accidental trauma.** Characteristic child abuse injury patterns include looped cord marks, belt buckle-shaped lesions, multiple bruises in various stages of healing, hand prints, bite marks, and circumferential cord marks around the neck from strangulation. Burn injuries may resemble the insulting object, such as a steam or curling iron. **Intentional hot water immersion usually leaves a sharply demarcated border; the "stocking glove" distribution is a classic pattern.** Cigarette burns are circular and may appear similar to impetigo or insect bites.

The differential diagnosis of multiple ecchymoses includes hemophilia, immune (idiopathic) thrombocytopenic purpura (ITP), Henoch-Schönlein purpura (or other vasculitis), and disseminated intravascular coagulation (DIC). Patterned injury can result from folk medicine practices, such as cupping (a heated cup applied to the skin leaves a circular injury) or coin rubbing (leaves linear red marks on the back). A history, physical examination, and a few screening tests can help eliminate these diagnostic considerations.

Skeletal injuries suspicious for abuse include long bone metaphyses injuries, rib or complex skull fractures, and multiple fractures (especially

those in various stages of healing). Spiral or oblique long bone fractures can result from unintentional rotating force injuries; they are no longer considered diagnostic of abuse. Nursemaid's elbow (radial head subluxation) occurs accidentally when a toddler falls while walking and holding an adult's hand (elbow dislocation occurs as the limb is pulled and twisted). Osteogenesis imperfecta, scurvy, cortical hyperostosis, and Menkes kinky hair disease are rare pediatric conditions with increased risk of bony injury.

## COMPREHENSION QUESTIONS

- 58.1 A 2-year-old boy presents 4 hours after a left arm injury. He tried to run into the street, and his mother held his left hand tightly and he fell. Since then he has not moved his arm. Now he holds the arm close to his body with the elbow flexed and the forearm pronated. The elbow is not erythematous or edematous. He cries when the elbow is touched. Which of the following is the best next step in management?
- A. Obtain a radiograph of the left elbow.
  - B. Order a skeletal survey.
  - C. Place the left arm in a sling.
  - D. Supinate the child's forearm while applying pressure over the radial head.
  - E. Apply traction to the forearm while increasing the degree of pronation.
- 58.2 A 15-year-old adolescent female has 2 days of nasal congestion and cough. Upon auscultation of her back, you find the lesions noted ([Figure 58-1](#)). Which of the following is the most likely etiology for her condition?



**Figure 58-1.** Picture of a child's back.

- A. Cupping
- B. Physical abuse
- C. Disseminated intravascular coagulation
- D. Henoch-Schönlein purpura
- E. Coining

**58.3** Which of the following describes the most common form of child maltreatment?

- A. Sexual abuse
- B. Physical abuse
- C. Neglect
- D. Emotional abuse
- E. Munchausen syndrome by proxy

**58.4** A 4-month-old girl is fussy, appears to have pain on palpation of the right leg, and has bluish sclerae. Radiographs reveal a right femur fracture. Her parents deny any severe trauma but report she had multiple fractures

as a child. Family history is also likely to include which of the following?

- A. Blindness
- B. Hearing loss
- C. Tall stature
- D. Renal disease
- E. Aortic aneurysm

## ANSWERS

- 58.1 D.** This child's history is consistent with a traction injury involving an outstretched arm. The elbow is not swollen and the arm is held in a flexed and pronated position. The child likely has "nursemaid's elbow." To reduce the subluxation, apply radial head pressure while supinating the arm. If treatment is not delayed, the child will usually begin using the arm promptly.
- 58.2 A.** This adolescent has multiple perfectly circular lesions on her back consistent with cupping; when asked, she gives the history of cupping. Physical abuse injuries likely would not be identical in appearance. Patients with DIC will have significant systemic manifestation, and the pattern of ecchymoses would not be symmetrical. Coining causes ecchymosis in a linear pattern.
- 58.3 C.** The most common form of child maltreatment is neglect (failure to provide adequate nutrition, shelter, supervision, or health care).
- 58.4 B.** This infant has features of osteogenesis imperfecta, an autosomal dominant genetic disorder most often caused by point mutations of COL1A1 or COL1A2. Features include long bone fractures and vertebral injury with minimal trauma, short stature, deafness, and blue sclerae. Four main types exist: type 1 is mild; type 2 is lethal (*in utero* or shortly thereafter); type 3 is the most severe; and type 4 is moderately severe. The recently described types 5-7 do not have mutations of type 1 collagen.

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## CLINICAL PEARLS

- All cases of suspected child maltreatment must be reported to Child Protective Services or law enforcement.
  - If the history of trauma does not fit a patient's injury pattern, child abuse is suspected.
  - If a child's development is inconsistent with the injury history, child abuse is suspected.
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A 2-year-old child suddenly develops inspiratory stridor, tachypnea, and chest retractions. He had been playing alone with his 6-year-old brother before this episode. He is afebrile. Apart from the stridor, his lung sounds are clear, and his physical examination is otherwise normal. A chest radiograph reveals no abnormalities.

- ▶ What is the most likely diagnosis?
- ▶ What is the next step in management of this patient?

### ANSWERS TO CASE 59: **Foreign Body Aspiration**

*Summary:* A 2-year-old child who was previously healthy experiences sudden onset of respiratory distress.

- **Most likely diagnosis:** Foreign body aspiration.
- **Next step in management:** The child's airway should be evaluated with bronchoscopy. Intravenous access should be established for administration of maintenance fluids and sedation for the procedure; the child should take nothing by mouth until his respiratory distress resolves. Oxygen saturation should be monitored closely.

## ANALYSIS

### *Objectives*

1. Recognize the signs and symptoms of childhood acute upper airway obstruction.
2. Know the differential diagnosis for childhood upper airway obstruction.
3. Know the principles of acute management of childhood upper airway obstruction.

### *Considerations*

This child's good health just prior to developing respiratory symptoms is a major clue to his diagnosis. Foreign body aspiration or anaphylactic responses to an allergen are the two most likely explanations for his sudden symptoms. The additional information that the child was playing alone with



another child suggests a scenario whereby the older child may have “shared” a toy, a piece of candy, or another enticing object with our patient. Stridor may be easily confused for wheezing by less experienced clinicians, which might lead one to also consider lower respiratory etiologies in the differential diagnosis. Stridor, however, is characterized by its monophonic sound (ie, a single pitch) that is louder over the upper chest. In contrast, wheezing represents blockage of multiple small airways and is heard as a polyphonic sound (ie, multiple pitches), heard best with the stethoscope placed over the lung bases.

APPROACH TO:

**Suspected Foreign Body Aspiration**

## DEFINITIONS

**STRIDOR:** A high-pitched, monophonic harsh sound that is usually inspiratory; it results from upper airway obstruction. The obstruction may be supraglottic (ie, above the vocal cords), glottic, and/or subglottic (ie, below the vocal cords).

**TACHYPNEA:** A respiratory rate that is faster than normal **for the person’s age**. The resting respiratory rate for an infant or young child is faster than that of an older person. The average resting respiratory rate for an infant is 30 breaths/min, whereas an 8-year-old child breathes at 20 breaths/min, and an adult breathes at a rate of approximately 16 breaths/min.

**DYSPNEA:** A subjective difficulty in breathing. Patients may describe it as feeling “short of breath.”

**ATELECTASIS:** Collapse of a portion of the lung. Atelectasis may be due to intrinsic factors, such as blockage of the airway proximal to the atelectatic tissue, or extrinsic factors, such as a pneumothorax.

## CLINICAL APPROACH

**Foreign body aspiration is a common cause of respiratory distress in young children and is a major cause of morbidity and mortality in this age group.** Children younger than 3 years of age typically explore their

environment by putting objects in their mouths. Commonly aspirated objects include nuts, popcorn, seeds, raw carrot and hot dog pieces, grapes, candies, small toys, and coins. Objects that lodge in the larynx or trachea can cause rapid asphyxia and death if not dislodged immediately. These usually present with respiratory distress, cough, and stridor; aphonia (“hoarseness”) may also be present. More commonly, objects lodge in a bronchus and present with cough, wheezing, and decreased breath sounds over the affected side.

Atelectasis or pneumonia may later develop. About 20% of cases are not diagnosed until 1 month after the incident, since an aspirated foreign body in the bronchus can mimic other causes of chronic cough and wheezing. Foreign bodies in the esophagus may also induce respiratory symptoms through pressure exerted on the membranous trachea. A carefully obtained history describing the **child’s state just prior to the onset of symptoms, physical examination, and a complete review of systems is key** to making the correct diagnosis. Bronchoscopy should be performed if these suggest aspiration **even if x-rays are normal.**

The general differential diagnosis for a child with stridor, tachypnea, and chest retractions includes infectious and other noninfectious etiologies. A child with fever, hoarseness, a “barky” cough, and a recent history of rhinorrhea or congestion may have **croup (laryngotracheobronchitis)**. A variety of viruses have been implicated, the most common being parainfluenza. X-ray of the neck may show a **tapered subglottic airway (“steeple sign”)**. **Epiglottitis** (rare as a result of widespread *Haemophilus influenzae* vaccination) is identified by its characteristic clinical signs: **drooling, a preference to sit in a tripod or upright position (“sniffing” position), muffled vocalizations, inspiratory stridor, and absence of cough.** Identification of epiglottitis is crucial because the high risk for sudden complete airway obstruction necessitates immediate care. **Bacterial tracheitis** caused by *Staphylococcus aureus* (or less commonly *Moraxella catarrhalis* or nontypeable *H influenzae*) can occur as a sequela 5 to 7 days after viral croup. Like epiglottitis, bacterial tracheitis can cause life-threatening airway obstruction and thus may require emergent intubation or tracheostomy. **Noninfectious causes** mimicking foreign body aspiration include **retropharyngeal abscess, angioedema, tracheomalacia, extrinsic airway compression (aortic/vascular ring, tumor), and intraluminal obstruction (papilloma, hemangioma).** The term *spasmodic croup* is used to describe the syndrome of sudden nighttime onset of hoarseness, “barky”

cough, and inspiratory stridor in a previously healthy, afebrile child. Viral infections, respiratory allergies, gastroesophageal reflux, and psychosocial factors are implicated as possible etiologies for spasmodic croup.

Some aspirated objects (eg, a metal coin) are easily visualized on radiographs, and their appearance indicates their location. Coins lodged in the trachea appear as a line on the AP radiograph because the cartilaginous rings on the anterior side of the trachea force the coin into this position. Coins in the esophagus result in dysphagia and milder respiratory symptoms; they appear as circles on AP radiograph. **Objects that are small enough to pass beyond the carina most typically lodge in the right mainstem bronchus,** because it is more vertical than the left bronchus. Objects made of plastic and other radiolucent materials are not visible on radiographs, although there may be other radiographic clues, such as air trapping where the obstructed lung remains inflated on a PA expiratory film and the mediastinum may be shifted toward the normal lung's side. Rigid bronchoscopy is diagnostic and therapeutic in cases of foreign body aspiration into an airway; endoscopy can be used if the object is in the esophagus.

## COMPREHENSION QUESTIONS

- 59.1 A 7-month-old boy with respiratory difficulty is brought to the emergency department at 3 AM. His mother reports that several family members have had “colds” over the past week. He first developed cough and coryza 3 days ago, and the cough has become “barky.” On examination, he has an axillary temperature of 100.4°F (38°C), respiratory rate 55 breaths/min, and heart rate 140 bpm (beats/min). A moderately inflamed pharynx and inspiratory stridor are noted on physical examination. Which of the following is the next step in management of this patient?
- A. Reassure the child's parents that his upper respiratory symptoms will resolve without antibiotics or other medication.
  - B. Obtain a chest radiograph.
  - C. Obtain a throat swab specimen for rapid testing for *Streptococcus pyogenes*.
  - D. Administer aerosolized racemic epinephrine and corticosteroids immediately.

E. Obtain blood, urine, and cerebrospinal cultures, and begin parenteral antibiotics.

59.2 A 14-month-old girl has a 6-hour history of fever to 102.6°F (39.2°C) and an increasingly ill appearance. She is anxious and does not want to leave her mother's arms, but she gives only a faint cry when approached. Her respiratory rate is 70 breaths/min and her neck is hyperextended. An area of moisture is noted on the shoulder of the mother's blouse. Which of the following is the next most appropriate step in management?

A. Perform a complete physical examination with particular emphasis on the mouth and upper airway.

B. Immediately secure the airway with an endotracheal tube in the emergency department.

C. Arrange for immediate transfer to the operating room to secure the airway through tracheal intubation or tracheostomy.

D. Administer aerosolized racemic epinephrine and nebulized steroids.

E. Obtain blood, urine, and cerebrospinal cultures, and begin parenteral antibiotics.

59.3 A 2-year-old boy is seen in your clinic after his parents report a "rough night." Following a few days of mild upper respiratory symptoms but no fever, last night he had an episode of stridor and increased effort of breathing. He has done this twice previously in the last 2 months and was well before each episode. In the interim period he has been normal. Today, apart from some mild rhinorrhea, his physical examination is normal. Which of the following is the most likely etiology?

A. Spasmodic croup

B. Foreign body aspiration

C. Tracheomalacia

D. Extraluminal compression of the trachea by a tumor

E. *S. pyogenes* pharyngitis

59.4 A 2-year-old boy with a 3-day history of upper respiratory congestion and cough now has inspiratory stridor, respiratory rate of 50 breaths/min, chest retractions, and a fever of 101°F (38.3°C). The next step in the management of his condition should be which of the following therapies?

- A. Pseudoephedrine and dextromethorphan
- B. Albuterol and cromolyn
- C. Ampicillin and gentamicin
- D. Cool mist and herbs
- E. Aerosolized racemic epinephrine and steroids

## ANSWERS

- 59.1 D.** This child's history and physical examination findings are typical of croup. Croup often presents at night when symptoms typically worsen. Cool mist is often used in an attempt to relieve laryngeal spasm; the evidence supporting its effectiveness is weak except in cases of allergic (spasmodic) croup. Aerosolized epinephrine and oral or aerosolized steroids are effective in reducing airway edema and relieving croup symptoms. Potentially irritating procedures (ie, use of tongue blades or needle sticks) are avoided unless necessary; agitation and crying aggravate the respiratory symptoms. Parenteral fluids rarely may be indicated if the child is not drinking well. Oxygen saturation should be monitored closely; a low saturation in croup indicates imminent airway obstruction.
- 59.2 C.** This child's clinical picture is consistent with epiglottitis, a medical emergency. She is kept calm and is transported to an operating room where the airway is examined and secured by a surgeon and anesthesia team skilled in tracheal intubation and tracheostomy. Visualizing the pharynx in the emergency department may cause airway obstruction. Although rare in the United States, epiglottitis occasionally is seen in hypoimmunized children or as a result of infection with *S pyogenes*, *S pneumoniae*, or *S aureus*.
- 59.3 A.** Children with spasmodic croup appear well during the daytime but develop nocturnal stridor and difficulty breathing; the cause is unknown. As this child's symptoms resolved during the daytime and he previously has had two similar episodes, foreign body aspiration is less likely (although always considered in a toddler with respiratory distress). Infants with mild tracheomalacia have stridor only intermittently (eg, with crying), but it is first noted in early infancy. A tumor compressing the

trachea usually causes persistent or progressive symptoms but less likely intermittent stridor. Streptococcal pharyngitis causes fever and throat pain but generally not significant stridor.

- 59.4 E. Aerosolized epinephrine and steroids are the only therapies that significantly improve symptoms of croup (in this case, likely viral). Systemic and nebulized steroids also reduce hospital admissions, length of hospital stay, and hospital readmission.
- 

## CLINICAL PEARLS

- Foreign body aspiration should be considered in the differential diagnosis for a previously healthy young child with sudden onset of stridor and respiratory distress, as well as for a previously healthy child with chronic cough or wheezing.
  - The differential diagnosis of foreign body aspiration also includes croup, epiglottitis, bacterial tracheitis, tracheomalacia, extrinsic airway compression, and other forms of intraluminal obstruction. Epiglottitis and bacterial tracheitis require stabilization in a calm environment by an expert skilled in airway management. Asthma and other forms of chronic obstructive pulmonary disease should be considered for the child with wheezing.
  - Aspirated objects that pass beyond the carina usually lodge in the right mainstem bronchus.
  - Rigid bronchoscopy is both diagnostic and therapeutic in cases of foreign body aspiration.
- 

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## CASE 60

A 3-year-old boy presents for his second visit to see you. Two days ago he was seen with a 4-day history of intermittent fever spiking to 104°F (40°C) and irritability. His examination at that time was remarkable for bilateral conjunctivitis, oropharyngeal injection, and red cracked lips. He drank 4 oz of an electrolyte solution in the clinic and was sent home with instructions for symptomatic care. Today he returns with persistent fever and irritability. The physical findings noted previously are still present, but now he also has a maculopapular truncal rash, hand and foot edema, and an enlarged but nonsuppurative right anterior cervical lymph node.

- What is the most likely diagnosis?
- What is the best diagnostic test for this disorder?
- What is the treatment for this condition?

## ANSWERS TO CASE 60: **Kawasaki Syndrome**

*Summary:* A 3-year-old boy with high-spiking fevers and irritability of 6 days' duration. Conjunctivitis, unilateral anterior cervical lymphadenopathy, oropharyngeal erythema, red cracked lips, a maculopapular rash, and edema of the hands and feet are present on examination.

- **Most likely diagnosis:** Kawasaki syndrome (KS; mucocutaneous lymph node syndrome).
- **Best diagnostic test:** No laboratory study is diagnostic. Echocardiography is used to monitor for coronary aneurysm development, the most serious potential disease complication. Elevated acute-phase reactants (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP]), normocytic anemia, and thrombocytosis support the diagnosis.
- **Treatment:** Early anti-inflammatory therapy with high-dose intravenous immunoglobulin (IVIG) and aspirin reduces the risk of coronary complications.

## ANALYSIS

### *Objectives*

1. Know the diagnostic criteria for KS.
2. Recognize the need for early diagnosis and treatment to prevent coronary complications.
3. Be familiar with other diagnostic possibilities in the differential diagnosis of KS.

### *Considerations*

Diagnosing KS can be difficult in the first few days of illness, when only a few classic clinical findings may be present. Adenoviral infection was perhaps the presumptive diagnosis at the first visit, although the intermittent fevers for 4 days and irritability might have prompted suspicions of another etiology. His diagnosis became more obvious on the sixth illness day when he manifested additional clinical signs, although other conditions still must be considered.

APPROACH TO:

**Fever and Rash**

## DEFINITIONS



**HYDROPS OF GALLBLADDER:** When the wall of the gallbladder becomes acutely distended without presence of stone or inflammation; commonly associated with KS, group A streptococcal infection, leptospirosis, or Henoch-Schönlein purpura.

**POLYMORPHOUS RASH:** An exanthem that may take various forms among affected individuals, such as maculopapular, erythema multiforme, morbilliform, or scarlatiniform.

**STRAWBERRY TONGUE:** Erythema of the tongue with prominent papillae, typically seen only in scarlet fever, KS, and toxic shock syndrome.

**THROMBOCYTOSIS:** Elevation of the platelet count above 450,000/mm<sup>3</sup>. In KS this usually occurs after the 10th day of illness and may last for a few weeks.

## CLINICAL APPROACH

**Kawasaki syndrome is a generalized vasculitic disease of medium-sized arteries associated with fever and exanthem of unknown etiology, but is thought to be infectious.** The incidence is highest among Asians, but it is seen worldwide. It occurs most frequently in **children younger than 5 years** and slightly more frequently in boys than in girls. It is the most common cause of acquired heart disease in American children.

The diagnosis of KS is based on finding the characteristic signs ([Table 60-1](#)), although children with fewer signs who later develop **coronary artery disease (CAD)** are recognized. Cervical adenopathy is seen less frequently than the other diagnostic criteria, occurring in 30% of patients; while **conjunctivitis** occurs in over 90% of the children. Incomplete disease occurs most frequently in infants, the group most likely to develop coronary complications. Although no test establishes the diagnosis, certain laboratory findings are characteristic. The **ESR and CRP are elevated**, and normocytic anemia and leukocytosis are common. The platelet count is usually normal initially but often rises above 500,000 by the 10th day. **Sterile pyuria, cerebrospinal fluid pleocytosis, and mildly elevated hepatic transaminase levels** are the most commonly seen abnormalities when other organ systems are involved. Other gastrointestinal symptoms may include abdominal pain, right upper quadrant pain, and vomiting (which can also be symptoms of

hydrops of the gallbladder). Patients can have arthralgias, arthritis, or anterior uveitis. Cardiac echocardiography may identify abnormalities of the coronary arteries, valves, pericardium (effusion), or myocardium (congestive heart failure). The differential diagnosis of KS includes infectious and noninfectious conditions, such as streptococcal disease, staphylococcal toxin (toxic shock syndrome), rickettsial infection, measles, Epstein-Barr virus infection, drug hypersensitivity reactions, systemic-onset juvenile idiopathic arthritis, and leptospirosis.

**Fever lasting for at least 4 days** (or fewer days if defervescence occurs in response to early IVIG therapy) in a child without evidence of other more likely pathology, plus the presence of at least four of the following five signs:

1. **Bilateral bulbar conjunctivitis**, generally without discharge
2. Oropharyngeal mucosal changes including **pharyngeal erythema, red cracked lips, and strawberry tongue** (see Figure 60–1)
3. **Polymorphous generalized erythematous rash** (usually most pronounced in the perineum where there may also be desquamation)
4. **Edema of the hands or feet and erythema of the palms and soles** in the acute phase; periungual desquamation in the subacute phase
5. **Acute nontender cervical lymphadenopathy** (usually unilateral and measures 1.5 cm or greater)

***Note:** Patients with fever and three of these criteria can be diagnosed with Kawasaki disease when coronary aneurysm or dilatation is recognized by 2-D echocardiography or coronary angiography.*

**Table 60-1 • DIAGNOSTIC CRITERIA FOR KAWASAKI DISEASE**



**Figure 60-1.** A child with Kawasaki disease with cherry red and hemorrhagic fissuring of the lips, an erythematous exanthema, and edema of the fingertips. (Reproduced, with, permission from Wolff K, Johnson RA. Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology. 6th ed. New York, NY: McGraw-Hill; 2009. Figure 14-44.)

Successful treatment depends on rapidly **starting high-dose aspirin and IVIG**. Rapid defervescence in the next 2 to 3 days generally occurs with this regimen. Aspirin therapy is later reduced from anti-inflammatory to antithrombotic doses and continued until 6 to 8 weeks after disease onset, when the ESR normalizes. Children with coronary artery disease require prolonged antithrombotic therapy.

**Even with treatment, approximately 5% of children develop coronary artery dilation, and 1% develop giant aneurysms.** Without treatment in the first 10 days, fever tends to persist and 25% of children will develop aneurysms. Aneurysm risk factors include male gender, prolonged fever, age younger than 12 months, higher baseline neutrophil and band counts, lower hemoglobin level, and platelet count less than  $350,000/\text{mm}^3$ . Children without known cardiac sequelae during the first month return to their normal state of health; those with persistent cardiac abnormalities may suffer significant morbidity. Death is rare and is caused by myocardial infarction or, less commonly, aneurysm rupture.

## COMPREHENSION QUESTIONS

- 60.1 A 12-month-old child arrives for a well-child examination. He was hospitalized 2 months ago for KS and was taken off aspirin therapy 6 weeks prior to this visit. His most recent echocardiogram was normal. For this patient, special consideration should be paid to which of the following?
- A. His developmental assessment
  - B. The abdominal examination
  - C. Live-vaccine administration
  - D. Serum hemoglobin evaluation
  - E. Assessment of possible lead toxicity
- 60.2 A 15-month-old child is on long-term aspirin therapy for coronary artery abnormalities that resulted from KS. In addition to his routine vaccinations required for school, he should receive which of the following?
- A. Pneumococcal vaccine
  - B. Influenza vaccine
  - C. Meningococcal vaccine
  - D. Oral polio vaccine
  - E. Varicella vaccine
- 60.3 A 5-month-old irritable infant develops 3 days of high fever, a maculopapular diaper rash, and swollen, red lips. He has a mild normocytic anemia and a white blood cell count (WBC) of  $15,000/\text{mm}^3$  with a predominance of neutrophils and immature forms. Urinalysis is normal, but the cerebrospinal fluid shows a pleocytosis with a negative Gram stain. After 24 hours of ceftriaxone, he continues to have high fever and has developed foot edema. Subsequent management of this child should include which of the following?
- A. Nystatin for the diaper rash
  - B. Repeat of the spinal tap
  - C. Addition of vancomycin to the antibiotic regimen

- D. Pediatric cardiology consultation; beginning of IVIG infusions and oral high-dose aspirin
  - E. Continuing current management and following the culture results
- 60.4 Who of the following children with KS is at greatest risk for coronary artery disease?
- A. A 5-year-old boy with 6 days of high fever, sterile pyuria, a truncal rash, and strawberry tongue
  - B. A 3-year-old girl with 5 days of high fever and cerebrospinal fluid pleocytosis
  - C. A 2-year-old girl with 5 days of high fever and an initial ESR of 80 mm/h
  - D. A 1-year-old boy with 6 days of high fever, a maculopapular rash, and mildly elevated hepatic transaminase levels
  - E. A 6-month-old boy with 11 days of high fever and a small pericardial effusion on initial echocardiogram

## ANSWERS

- 60.1 C. Live-virus vaccines (measles-mumps-rubella [MMR], varicella) are delayed for 11 months following high-dose IVIG administration; IVIG potentially interferes with the immune response. The measles vaccine, typically given as MMR at 12 months, is provided if the exposure risk is high, but reimmunization is required unless serologic testing indicates adequate antibody titers.
- 60.2 B. Children on prolonged aspirin therapy receive the influenza vaccine; they are at increased risk of Reye syndrome if they are infected and taking aspirin. Reye syndrome is composed of acute encephalopathy and liver dysfunction with one-third of affected children dying from the disease; it seemed to be linked to children with a viral illness, especially influenza, who took aspirin during the illness. While often not required for day care or school attendance, the Centers for Disease Control and Prevention recommends that all children aged 6 months and older receive an annual influenza vaccine.

- 60.3 **D.** This child's initial presentation is consistent with, but not diagnostic of, KS (Table 60-1). His persistent fever and peripheral extremity edema increase the possibility of KS and should prompt further investigation and treatment.
- 60.4 **E.** Risk factors for development of coronary aneurysms include male gender, fever for more than 10 days, age younger than 12 months, low serum albumin or hemoglobin level, early cardiac findings (eg, mitral regurgitation or pericardial effusion), and thrombocytopenia.
- 

### CLINICAL PEARLS

- The diagnosis of Kawasaki syndrome (KS) is based on clinical criteria and should be strongly suspected in a young child with a combination of high fever for more than 4 days, oropharyngeal changes, conjunctivitis, extremity changes, rash, and cervical adenopathy.
  - Children with incomplete disease ("atypical KS") can develop coronary artery abnormalities.
  - The most important complication of KS is coronary artery disease. A pediatric cardiologist usually is involved in the care of these children.
  - Early recognition and initiation of therapy for KS is key to preventing potential coronary complications.
- 

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## **SECTION III**

### **Listing of Cases**

[Listing by Case Number](#)

[Listing by Disorder \(Alphabetical\)](#)



## Listing by Case Number

CASE NO.	DISEASE
1	Failure to Thrive
2	Adolescent Substance Abuse
3	Down Syndrome
4	Immunodeficiency
5	Klinefelter Syndrome
6	Megaloblastic Anemia
7	Rickets
8	Diabetic Ketoacidosis
9	Sickle Cell Disease with Probable Stroke
10	Pneumonia
11	Organophosphate Poisoning
12	Rectal Bleeding
13	Acute Otitis Media
14	Neonatal Resuscitation
15	Cerebral Palsy
16	Cystic Fibrosis
17	Acute Lymphoblastic Leukemia
18	Infant of a Diabetic Mother
19	Gilbert Syndrome
20	Asthma Exacerbation

- 21 Growth Hormone Deficiency
- 22 Group B Streptococcal Infection
- 23 Sudden Infant Death Syndrome
- 24 Ventricular Septal Defect
- 25 Transposition of the Great Arteries
- 26 Juvenile Idiopathic Arthritis (JIA)
- 27 Macrocytic (Megaloblastic) Anemia Secondary to Vitamin B<sub>12</sub> Deficiency
- 28 Lead Toxicity
- 29 Acute Poststreptococcal Glomerulonephritis
- 30 Precocious Puberty
- 31 Ambiguous Genitalia
- 32 Primary Syphilis
- 33 Pityriasis Rosea
- 34 Bacterial Meningitis
- 35 Bacterial Enteritis
- 36 Appendicitis
- 37 Acute Epstein-Barr Viral Infection (Infectious Mononucleosis)
- 38 Pinworms
- 39 Subdural Hematoma
- 40 Dysfunctional Uterine Bleeding
- 41 Simple Febrile Seizure
- 42 Muscular Dystrophy
- 43 Neonatal Herpes
- 44 Atopic Dermatitis
- 45 Neuroblastoma

46	Retropharyngeal Abscess
47	Esophageal Atresia
48	Transient Tachypnea of the Newborn
49	Malrotation
50	Acne Vulgaris
51	Posterior Urethral Valves
52	Attention-Deficit/Hyperactivity Disorder
53	Osgood-Schlatter Disease
54	Torticollis
55	Congenital Cataracts
56	Severe Hearing Loss
57	Immune Thrombocytopenic Purpura
58	Child Abuse
59	Foreign Body Aspiration
60	Kawasaki Syndrome

## **Listing by Disorder (Alphabetical)**

CASE NO.    DISEASE

50	Acne Vulgaris
37	Acute Epstein-Barr Viral Infection (Infectious Mononucleosis)
17	Acute Lymphoblastic Leukemia
13	Acute Otitis Media
29	Acute Poststreptococcal Glomerulonephritis
2	Adolescent Substance Abuse
31	Ambiguous Genitalia
36	Appendicitis
20	Asthma Exacerbation
44	Atopic Dermatitis
52	Attention-Deficit/Hyperactivity Disorder
35	Bacterial Enteritis
34	Bacterial Meningitis
15	Cerebral Palsy
58	Child Abuse
55	Congenital Cataracts
16	Cystic Fibrosis
8	Diabetic Ketoacidosis
3	Down Syndrome
40	Dysfunctional Uterine Bleeding

47	Esophageal Atresia
1	Failure to Thrive
59	Foreign Body Aspiration
19	Gilbert Syndrome
22	Group B Streptococcal Infection
21	Growth Hormone Deficiency
57	Immune Thrombocytopenic Purpura
4	Immunodeficiency
18	Infant of a Diabetic Mother
26	Juvenile Idiopathic Arthritis (JIA)
60	Kawasaki Syndrome
5	Klinefelter Syndrome
28	Lead Toxicity
27	Macrocytic (Megaloblastic) Anemia Secondary to Vitamin B <sub>12</sub> Deficiency
49	Malrotation
6	Megaloblastic Anemia
42	Muscular Dystrophy
43	Neonatal Herpes
14	Neonatal Resuscitation
45	Neuroblastoma
11	Organophosphate Poisoning
53	Osgood-Schlatter Disease
38	Pinworms
33	Pityriasis Rosea
10	Pneumonia

51	Posterior Urethral Valves
30	Precocious Puberty
32	Primary Syphilis
12	Rectal Bleeding
46	Retropharyngeal Abscess
7	Rickets
56	Severe Hearing Loss
9	Sickle Cell Disease with Probable Stroke
41	Simple Febrile Seizure
39	Subdural Hematoma
23	Sudden Infant Death Syndrome
54	Torticollis
48	Transient Tachypnea of the Newborn
25	Transposition of the Great Arteries
24	Ventricular Septal Defect

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